Spring 2019

A Review of Equine Laminitis: Risk Factors and Predispositions

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Abstract

Equine laminitis is a disease of the hoof characterized by inflammation or disruption of the sensitive and insensitive laminae located within the hoof. These structures are responsible for maintaining a secure connection between the third phalanx (P3) and the hoof wall. Damage to these laminae can weaken the attachment between the hoof wall and P3, causing separation and eventual rotation of P3. Equine laminitis can result from multiple triggers, but the most commonly seen cases of the disease are those which are related to endocrinopathy and metabolic related issues. This review will focus on determining the metabolic risk factors associated with this disease, and what can be done to manage these animals. It has been shown that horses predisposed to developing endocrine or metabolic related laminitis are often characterized by a prior history of endocrine issues. They can also be affected by high serum insulin and triglyceride concentrations, as well as insulin resistance, often associated with diets high in non-structural carbohydrates. These horses have also been known to exhibit physical characteristics such as a body condition score of seven or greater and deposition of adipose tissue. Because laminitis is associated with high sugar intake, effectively managing the animal's diet is a key factor in mitigating the risk of developing the disease. It is also important to maintain proper hoof care and effectively manage pain to keep the animal comfortable.

A Review of Equine Laminitis: Risk Factors and Predispositions

Equine laminitis is a common disease of the hoof that can affect all equids. Recent studies suggest that the incidence of laminitis ranges from 1.5% to 34%, though many cases go unreported and undiagnosed by a veterinarian, meaning that the total number of cases is likely underestimated (Coleman et al., 2018, Pollard et al., 2018). Laminitis is characterized by inflammation of the laminae located within the hoof. These structures are responsible for maintaining a secure connection between the third phalanx (P3), commonly referred to as the coffin or pedal bone, and the hoof wall. Damage to and inflammation of the laminae result in a weakened connection, causing separation and rotation of the coffin bone. In the most severe cases, the coffin bone rotates to such an extent that it begins to penetrate through the sole of the hoof. Laminitis frequently affects mares more than geldings, and it has been shown that the likelihood of developing this disease increases with age (Alford et al., 2001). However, there is inconsistency in these findings, with other studies showing no correlation between age or sex and the development of laminitis (Polzer and Slater, 1997). This debilitating disease can result from a number of causes and triggers, and understanding these underlying causes will allow horse owners to develop appropriate management techniques to keep affected horses comfortable.

A horse experiencing a unilateral lameness not related to laminitis may develop the disease in the opposite hoof due to the increased weight bearing on that limb (Eades, 2010). It is also possible for an animal to develop sepsis induced laminitis. Horses diagnosed with various illnesses such as pneumonia, diarrhea, colic, or endotoxemia are known to have an increased concentration of toxins circulating the body. These toxins have the potential to negatively impact the laminae of the hoof, resulting in laminitis (Parsons et al., 2007, Eades, 2010). However, the most common cases of laminitis are due to due to endocrine or metabolic related issues, typically attributed to increased intake of lush pasture. As of 2007, pasture associated laminitis was

estimated to account for roughly 54% of all cases of equine laminitis (Anon, 2000). This review will seek to investigate the metabolic causes of this disease, identify common characteristics in at-risk animals, and determine what management strategies can be implemented to mitigate the risk of laminitis and ensure that affected animals are kept comfortable.

Metabolic Related Laminitis

The literature surrounding metabolic related laminitis tends to compare the disease to human medicine. In humans, metabolic syndromes that can put an individual at risk for developing type two diabetes mellitus or heart disease are characterized by insulin resistance, glucose intolerance, high triglyceride concentrations, high density lipoprotein concentrations, hypertension, and abdominal obesity (World Health Organization, 1999, National Institutes of Health, 2002). Medical professionals in the field of human medicine evaluate the combination of insulin resistance and the aforementioned characteristics to diagnose an individual as "prediabetic" (WHO, 1999). A 1988 study by Reaven defined metabolic syndrome as a collection of these risk factors, which are exacerbated by a diet that is rich in carbohydrates (Reaven, 1988). It is also suggested that the development of these risk factors is hereditary, passing on to offspring as an autosomal dominant trait (Kerem et al., 2001).

Equine researchers are seeking to develop a similar set of risk factors in horses that could serve as a predictor for the development of laminitis. One of the earliest cases evaluating insulin resistance in equines was completed by Coffman and Colles in 1983. This study evaluated insulin resistance in a group of six laminitic animals and compared it to that of a non laminitic control group. Animals received an intravenous injection of insulin, and multiple blood samples were obtained over a five hour period following the injection. Analysis of the blood samples showed that the laminitic animals were significantly less sensitive to insulin over multiple trials. (Coffmann and Colles, 1983).

While the results of the aforementioned study suggest a link between insulin resistance and laminitis, there are many additional characteristics that are associated with laminitis and may predispose an animal for the disease. A study was done in 2007 to determine these risk factors and evaluate their predictive power for developing laminitis. A herd of Welsh and Dartmoor ponies was divided into a testing group of animals with a previous diagnosis of laminitis (PL) and a control group of non laminitic ponies (NL). These ponies were evaluated at the beginning of March, turned out to pasture, and reevaluated during the first week of May. Researchers weighed and assigned a body condition score (BCS) on a scale from one to nine, one being emaciated and nine being extremely obese, for each animal. Blood samples were also taken to evaluate concentrations of glucose, insulin, triglycerides, nonesterified fatty acids (NEFA), and cortisol. Insulin sensitivity was calculated using the reciprocal of the square root of insulin (RISQI) and insulin secretory response was calculated using a modified insulin-to-glucose ratio (MIRG) (Treiber et al., 2006). At the initial evaluation of the animals in March, the ponies in the NL group displayed an average BCS of 5.8 while the PL group showed a significantly higher average BCS of 6.4. These animals also exhibited deposition of adipose tissue along the crest of the neck, shoulders, ribs, and tail head. These results continued when the ponies were reevaluated at the beginning of May, with the PL group showing a significantly higher BCS than the NL group (Treiber et al., 2006).

Evaluation of the blood samples taken in March revealed that the concentrations of insulin and triglycerides were significantly higher in the PL ponies than the NL ponies. Concentrations of cortisol were significantly lower in PL ponies than NL ponies, and there was no significant difference between the concentrations of NEFA or glucose between the groups. The values obtained for insulin sensitivity were significantly lower in PL ponies when compared to the NL group, and the insulin secretory response was significantly higher in PL ponies than

NL ponies, indicating insulin resistance in PL ponies. These results were true of the samples taken in May as well, though it is important to note that an additional testing group was established at this time for animals that had developed clinical laminitis (CL). These animals were characterized by "reluctance to move, bounding digital pulses, and increased temperature of the hoof surface," (Treiber et al., 2006). Animals in the CL group showed concentrations of insulin and triglycerides that were significantly higher than those of either the PL or the NL group. The insulin sensitivity values for the CL group were significantly lower than those of the PL and NL groups, and the insulin secretory response for this group was significantly higher when compared to the PL and NL groups, indicating insulin resistance (Treiber et al., 2006).

Researchers determined that a combination of three or more of the following risk factors classify an animal as being affected by prelaminitic metabolic syndrome (PLMS): insulin resistance, compensatory insulin secretory response, hypertriglyceridemia, and obesity characterized by a BCS of six or greater with deposition of adipose tissue on the neck and tail head. Statistical analysis of the data obtained in this study shows that individual risk factors had a 70% predictive power for predicting laminitis, with the combination of three or more factors having a predictive power of 78% (Treiber et al., 2006).

The results of this study were corroborated by Carter and colleagues in 2009. Ponies were grouped into the PL testing group and the NL control group. Each animal was assigned a BCS on a scale of one to nine, and measurements were recorded for height at withers, girth circumference, waist circumference, and neck circumference. Animals were also given a cresty neck score (CNS) on a scale of one to five based on adiposity. Data were also recorded for blood pressure and hoof surface temperature. Blood samples were collected and evaluated for concentrations of glucose, triglycerides, uric acid, insulin, leptin, cortisol, adrenocorticotropic hormone (ATCH), and tumor necrosis factor alpha (TNFα). Researchers also used RISQI to

determine insulin resistance and MIRG to measure insulin secretory response. Results were analyzed to determine the predictive power of each characteristic. The results of this study concluded that animals can be characterized by PLMS based on the following criteria: a BCS of seven or greater, a CNS of four or greater, and RISQI of less than 0.17 $[mu/l]^{-.05}$ (Carter et al., 2009). Similar to the Treiber study, six animals from the PL group began to show clinical signs of laminitis throughout the course of the study and were placed into a CL group. Analysis of the data suggests that the following characteristics have the potential to predict clinical laminitis: BCS of seven or greater, CNS of four or greater, basal insulin concentration of greater than 32 mu/l, and leptin concentrations of greater than 7.3 ng/ml (Carter et al., 2009). These results are consistent with the findings of Bailey et al in 2007. In this study, researchers evaluated insulin sensitivity in a test group of animals that had previously experienced acute pasture associated laminitis, and compared the findings to a non laminitic control group. The data show that the laminitic animals are characterized by significantly greater insulin resistance than the non laminitic control animals (Bailey et al., 2007).

These results were again corroborated in an additional study evaluating insulin resistance in pony breeds native to the United Kingdom. Animals were divided into a test group of those that had experienced at least one episode of acute laminitis within three years prior to the study, and a non laminitic control group. Each animal was assigned a BCS on a scale of one to nine. Animals were also measured to determine body weight, height at withers, neck circumference, and height and thickness of adipose tissue along the crest of the neck. Measurements were recorded for blood pressure, and blood samples were obtained to evaluate concentrations of insulin, ACTH, glucose, triglycerides, and uric acid. Insulin resistance was calculated using RISQI and insulin secretory response was determined using MIRG. Each animal was initially

evaluated at the beginning of winter, and reevaluated at the beginning of summer (Bailey et al., 2008).

During the initial winter evaluation the non laminitic animals showed an average BCS of 5.63, compared to an average of 5.42 in the laminitic group. During the summer evaluation these averages increased to 5.78 and 5.51 respectively. Statistical analysis shows no significant difference between these figures. However, the results did show that the laminitic animals had significantly higher blood pressures than the control group during the summer, with no significant difference seen between groups during the winter. The summer testing also resulted in significantly higher insulin, triglycerides, and uric acid concentrations in laminitic ponies when compared to the control. Measurements for insulin sensitivity were significantly lower and measurements for insulin secretory response were significantly higher in laminitic ponies during the summer test, showing insulin resistance in these animals (Bailey et al., 2008).

A similar study conducted by Coleman and colleagues sought to determine the risk factors for pasture and endocrinopathy associated laminitis (PEAL). Horses were selected to participate in this study based on a veterinarian diagnosis of PEAL, bilateral forelimb lameness, sensitivity to hoof testers in the toe region, and the stereotypical “sawhorse” stance (Coleman et al., 2018). Two control groups were defined as healthy controls and lameness controls. Animals were categorized as lameness controls if they experienced a unilateral forelimb lameness of grade three or higher for no more than a four week period, and had no previous history of laminitis (Coleman et al., 2018).

Researchers collected data from each animal involved in the study to determine the horse’s age, breed, and sex, as well as its workload. Data were also collected for each horse’s housing environment, exposure to pasture, and diet. Each horse was assigned a BCS on a scale from one to nine, one being emaciated and nine being extremely obese. Measurements were

taken for the horse's height at the withers, as well as the circumference of the girth, waist, and neck. The presence or absence of adipose tissue was noted, particularly at the areas of the tail head, ventrum, flank, thoracic region, periorbital region, and crest of the neck. It was also noted if the animals had a history of pituitary pars intermedia dysfunction (PPID), equine metabolic syndrome, or obesity. Each horse's hoof care was also noted, along with history of corticosteroid administration, and recent transportation. For each horse diagnosed with PEAL, the season in which clinical signs began was also noted (Coleman et al., 2018). When comparing the data between the PEAL group and the healthy control group, analysis showed that animals with a BCS of seven or greater had a greater chance of developing PEAL, as did animals with general or regional deposition of adipose tissue, or a preexisting endocrinopathy or metabolic condition. The data also show that the onset of clinical signs of PEAL occurred most often in the spring and summer months rather than the fall and winter months (Coleman et al., 2018). Data analysis also shows a significant more likelihood of developing PEAL in ponies and miniature horses rather than Paint Horses, Quarter Horses, and Appaloosas. The likelihood of developing PEAL in Thoroughbreds, draft horses, and warmbloods appeared lower than Paint Horses, Quarter Horses, and Appaloosas, though this difference was not considered significant (Coleman et al., 2018).

It is apparent that insulin resistance is linked to the development of equine laminitis. A widely accepted definition was given by Kahn in 1978 to say that insulin resistance occurs "whenever normal concentrations of hormone produce a less than normal biologic response," (Kahn, 1978). It is possible for insulin resistance to develop as a result of disturbances with hormone receptors at the surface of the cell as well as within the cell (source 8). RISQI and MIRG can be used to determine insulin sensitivity and insulin secretory response respectively. These values can be used to determine insulin resistance within the horse. Low RISQI values indicate an insensitivity to insulin. This is typically accompanied by a higher MIRG value,

showing an exaggerated and compensatory secretion of insulin due to insulin resistance (Treiber et al., 2006). In humans, insulin resistance contributes to reduced glucose availability to cells, vasoconstriction, endothelial damage, and inflammatory response. In the horse, these processes encourage the hoof separation characteristic of laminitis. Insulin also acts as a vasodilatory hormone. However, an insulin insensitivity can compromise this effect, resulting in failure to combat vasoconstriction associated with endothelial damage (Treiber et al., 2006).

The PLMS phenotype consisting of increased adiposity, particularly with depositions along the crest of the neck, shoulders, ribs, and tail head, is said to be related to "thrifty genes" (Johnson et al., 2009). Due to the herbivorous nature of the horse as a species, animals are naturally presented with periods of food scarcity during the lack of forage growth characteristic of the winter months. As horses have been domesticated and cared for by humans, this food shortage has become less problematic. However, it has played a large role in the horse's evolution. Thrifty genes are thought to be responsible for increased deposition of adipose tissue as a result of increased forage intake, allowing the body to store energy to be used during times of food scarcity. Thus, prior to domestication, equids would prepare for the winter months by increasing their food intake and building up fat stores on the body, increasing their chances of survival. It is thought that the ability to accumulate adipose tissue is related to the development of insulin resistance (Johnson et al., 2009). Adipose tissue also has an effect on metabolic and vascular functions due to the production of leptin, TNFα, and other proinflammatory cytokines (Eades, 2010). Circulation of these substances can further contribute to insulin resistance (Suagee et al., 2012). Animals that are prone to developing this phenotype are thought to have inherited these thrifty genes. Animals used in the Treiber study that experienced clinical laminitis and PLMS were able to be traced back to common ancestors. This suggests that the development of laminitis and metabolic related issues has the potential to be passed on to

offspring through genetic inheritance. However, more research is needed in this area in order to confirm this theory (Treiber et al., 2006).

Nutritional Factors

It is widely accepted among researchers and equine professionals that an animal's diet plays a role in the development of laminitis. Administration of high concentrations of carbohydrates such as starch and fructan have been known to experimentally induce laminitis in equines (Garner et al., 1977, Pollitt et al., 2003). Due to the fact that these substances, among other carbohydrates, are contained within pasture grasses, it is likely that cases of laminitis are higher in predisposed animals that are kept at pasture. Pollitt et al. observed that a dosage of 3.75 kg of fructan resulted in the development of laminitis (Pollitt et al., 2003). Fructan is a carbohydrate that accumulates in cool season pasture grasses, which often provide a forage source for many equines. A number of studies have been done involving fructan and evaluating the carbohydrate content of pastures. In addition to evaluating insulin resistance, the 2006 Treiber study sampled and analyzed the pasture for starch and sugar content. Samples were analyzed by the Dairy Herd Improvement Association, and showed a significantly greater starch content in the samples obtained in May when compared to the samples obtained in March (Treiber et al., 2006) This finding may contribute to the increased insulin resistance seen in laminitic animals at this time. The 2007 study by Bailey et al. also evaluated the effects of fructan on insulin concentrations. Animals were kept on pasture for a minimum of two weeks before being removed from the pasture and fed a diet of timothy hay. Blood samples were collected prior to the start of the hay diet as well as one, two, five, and seven days after beginning the hay diet. The pasture and the hay were also sampled and analyzed for carbohydrate content. Control ponies showed no significant changes in insulin concentrations when transitioning from the pasture to the hay diet. In contrast, the laminitic animals showed

significantly higher insulin concentrations than control animals before starting the hay diet. These values also showed a significant decrease after beginning the hay diet, to such an extent that they were not significantly different from the control animals by day seven of the hay diet. Analysis of the pasture showed a fructan content of 138 g/kg of dry matter (DM), while the timothy hay showed a fructan content of only 34 g/kg DM. Total water soluble carbohydrates (WSC) were 182 g/kg DM and 66 g/kg DM for pasture and hay respectively (Bailey et al., 2007).

Researchers involved with this study also evaluated the effects of inulin, a commercially available form of fructan, on insulin concentrations. Animals were fed a diet of hay over a course of two weeks, at which point 3 g/kg inulin was added to the diet, split over three separate meals. Blood samples were taken before and after the addition of inulin and evaluated for insulin concentrations. Control ponies displayed a slight increase in insulin concentrations with the addition of inulin, though this increase was not found to be significant. In contrast, laminitic ponies showed a significant increase in insulin concentrations with the addition of inulin to the diet (Bailey et al., 2007).The findings of this study suggest that the increased intake of carbohydrates exacerbates the effects of insulin resistance in affected animals, but has little effect on healthy individuals. This is in congruence with the findings of Reaven in 1988.

It is evident that carbohydrate intake has implications in the development of insulin resistance, laminitis, and other metabolic related issues. This fact presents a set of challenges as the carbohydrate content of the forages fed to equines is dependent on a variety of factors. Sugars and carbohydrates are produced as a result of photosynthesis. They are utilized as fuel for the plant during times of growth and productivity, but are also produced in excess and stored until needed. Therefore, the carbohydrate content of a plant can vary depending on the productivity of the plant at a given moment (Longland and Byrd, 2006). Since carbohydrate production is dependent upon photosynthesis and the presence of sunlight, fluctuations in plant

carbohydrate content have been observed throughout the course of a day. A typical pattern shows carbohydrate contents increasing during the morning hours, reaching a maximum in the late afternoon and early evening, and declining overnight (Longland et al.,1999, Holt and Hilst, 1969, Bowden et al., 1968). It is also known that carbohydrate concentrations vary seasonally as the productivity of the plant fluctuates. Typically, carbohydrate concentrations are highest late spring, intermediate during the autumn months, and lowest mid-season (Waite and Boyd,1953). In addition to daily and seasonal fluctuation, plant carbohydrate content can be impacted by other environmental factors. Conditions that inhibit plant growth and productivity but do not impact photosynthesis result in higher concentrations of carbohydrates. In contrast, conditions which promote plant growth result in lower concentrations of carbohydrates (Longland and Byrd, 2006). For example, the environmental temperature can drop below an appropriate range for plant growth, but photosynthesis will continue to produce starch and sugars. It has been shown that the fructan content of a plant can be as low as 23 g/kg DM at temperatures falling between five and ten degrees Celsius, and as high as 439 g/kg DM at temperatures between 15 and 25 degrees Celsius (Chatterton et al., 1989). Similarly, light intensity can impact the concentration of carbohydrates. Research has determined that shading pastures of canary grass species for an average of 43 hours resulted in non-structural carbohydrate (NSC) contents of 62 g/kg DM, while an unshaded pasture contained NSC values of 126 g/kg DM (Volaire and Lelievre, 1997). Due to the extreme variations in pasture carbohydrate content, determining the carbohydrate consumption of an animal can prove to be a challenge. Reports of pasture intake by equines range from 1.5% to 5.2% of the horse's body weight (BW) per day (Marlow et al., 1983, McMenniman, 2000). With these degrees of consumption it is possible for an average 500 kg horse to consume at least 0.75 kg WSC/d, and up to 5-10 kg WSC/day for horses consuming 2.5% and 5.2% BW/d respectively. When isolating the fructan consumption, this translates to 3.5

kg fructan/day, only slightly lower than the 3.75 kg fructan used to induce laminitis by Pollitt, and 7.3 kg fructan/day, nearly double the amount used to induce laminitis. However, it should be noted that these levels of fructan are consumed gradually throughout the course of an entire day, whereas the fructan used to experimentally induce laminitis was administered via bolus. It is possible that this gradual increase allows gut bacteria time to adjust to the increased carbohydrate, reducing the chances of digestive upset and related issues (Longland and Byrd, 2006). It should also be noted that the findings of Myer et al. and Potter et al. recommend that maximum of 2 and 4 g starch/kg BW respectively be fed in a single meal (Meyer et al., 1995, Potter et al., 1992). For an average 500 kg horse, this translates to 2 and 4 kg starch/day, again similar to the 3.75 kg fructan used to induce laminitis (Longland and Byrd, 2006).

Management Strategies

There are a variety of management strategies that can be used to mitigate the effects of laminitis in predisposed animals, as well as to combat the chances of a healthy animal developing PLMS. Due to the fact that laminitis is linked to increased consumption of pasture and carbohydrates, the overarching goal of managing at-risk animals is to limit the intake of carbohydrates. This can be done through a number of techniques to manage pastures as well as animals. Pastures can be managed to effectively reduce the amount of carbohydrates present in the plant. Pastures should contain plant species that have been shown to accumulate lower concentrations of carbohydrates, soil fertilization and water quality should be maintained to promote adequate plant growth, and pasture grasses should be kept short through mowing or grazing (Longland and Byrd, 2006). Pasture and hay should also be sampled and analyzed to determine the carbohydrate content and nutritional value, and these results should be taken into consideration when developing rations based on the energy needs of individual animals.

Special consideration should be taken when managing animals that are predisposed to or affected by laminitis. Limiting the carbohydrate intake of these animals can be done by feeding a diet of primarily hay rather than pasture. Analysis of forage samples has shown that carbohydrates tend to be significantly reduced in timothy hay when compared to pasture grasses (Bailey et al., 2007). The amount of grain concentrates fed to these animals should also be limited. Horses find sugar to be highly palatable, and many feed companies use this to their advantage, increasing the sugar and starch content of the feed. Therefore, feeding these concentrates to predisposed animals should be avoided (Longland and Byrd, 2006). Limiting the intake of carbohydrates by animals turned out on pasture can be done by employing the use of grazing muzzles on at-risk animals. These muzzles minimize the consumption of pasture and carbohydrates while still allowing the animal to be turned out with its herd. Affected animals can also be turned out on pasture during the early morning hours when starch contents in pasture grasses are lowest, or they can be turned out in dry lot paddocks.

Because insulin resistance and the development of laminitis has been related to BCS and adiposity of individuals, an appropriate body weight should be maintained to lessen the metabolic effects related to obesity. This can be done by implementing and following an effective diet and exercise program. The energy needs of each animals should be determined based on their basal metabolic rate and workload. Guidelines established by the National Research Council recommend the digestible energy requirements of an average horse to be 0.0333 Mcal/kg BW. For an average 500 kg horse this translates to roughly 16.7 Mcal/day, and can be altered based on the intensity and duration of work typically performed by the animal. This calculation should be considered when sampling pasture and hay for nutrient analysis. The results of the forage analysis should be considered in relation to the energy needs of a particular animal and an appropriate feeding program should be developed based on these findings.

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