

Advances in the Identification of Increased Endocrinopathic Laminitis Risk and Disease Prevention

Endocrinopathic laminitis is the most common form of this clinical syndrome, accounting for up to 90% of cases. Identification of animals at an increased risk is vital to allow targeted implementation of preventative management strategies focusing on weight control and carbohydrate intake by owners. Recent publications by researchers at the Royal Veterinary College have demonstrated that at-risk animals can be identified using a high-dose oral sugar test and by measuring circulating concentrations of the adipose tissue derived hormone adiponectin. In addition, they have shown that disease prevention can be aided by the use of a weight loss tracking app and that strip grazing does not have a negative effect on physical activity.

What is Endocrinopathic Laminitis?

Laminitis is a common and painful condition of the adult equine, often resulting in permanent lameness or euthanasia. Reported estimates of laminitis frequency range from 1.5–34%,¹ depending on the population studied (general practice or referral institutions), proportion of ponies versus horses, presence of intercurrent diseases (particularly gastrointestinal disease) and the geographic location (generally USA, UK or Australia). It may occur as a single episode or, more commonly, as repeated bouts over a prolonged period (recurrent laminitis). The risk of all-cause mortality was increased nearly six-fold by the presence of laminitis in a population of horses treated in first opinion practices in the UK (hazard ratio 5.94 vs. no chronic disease), indicating the importance of this disease.¹

Laminitis is now considered to be a clinical syndrome associated with systemic disease (sepsis or systemic inflammatory response syndrome [SIRS] or endocrine disease) or altered weight bearing, rather than being a discrete disease entity.² Thus, laminitis can be divided into three forms, namely sepsis-associated, endocrinopathic, and supporting limb laminitis. Endocrinopathic laminitis is the most common form of laminitis, accounting for 90% of cases of laminitis in some studies.^{3,4} It encompasses laminitis linked with insulin dysregulation (ID), as occurring in association with the two common equine endocrine disorders; equine metabolic syndrome (EMS) and pituitary pars intermedia dysfunction (PPID). EMS is a collection of risk factors for laminitis, the most important of which is ID; additional features include adipose tissue dysregulation, resulting in altered production of adipose tissue derived hormones known as adipokines such as adiponectin, and obesity.⁵ PPID is a progressive neurodegenerative disorder associated with loss of the inhibitory dopaminergic input to the pituitary pars intermedia (PI).⁶ This results in increased production of the normal hormone products of the PI. Some of these hormones may antagonise the actions of insulin resulting in ID in a subset of animals with PPID^{7,8} and this appears to be associated with an increased risk of laminitis⁹ and a worse prognosis.¹⁰ Thus, identification of animals at an increased risk of endocrinopathic laminitis firstly relies on detection of insulin dysregulation.

Identifying Insulin Dysregulation

The term insulin dysregulation is used to indicate

disturbance of the balanced inter-relationship among plasma concentrations of insulin, glucose, and lipids.⁵ ID in the horse can manifest in several ways including one or more of basal hyperinsulinaemia, an excessive insulin response to oral carbohydrate consumption or tissue insulin resistance.¹¹ Thus, ID is identified in an individual animal by:

1) Measurement of basal serum insulin concentrations to detect basal hyperinsulinaemia

An indication of ID can be based on finding resting (or basal) hyperinsulinemia.¹² Basal insulin concentrations are increased in laminitis-prone animals¹³ and we have demonstrated that basal hyperinsulinaemia is associated with an increased risk of the development of laminitis for the first time in healthy animals.¹⁴ However, this test is affected by age, breed, exercise, stress, disease, feeding and diet. It has high specificity, but low sensitivity, and is only useful in identifying the most severely affected animals. Thus, dynamic testing is preferentially recommended.

2) Dynamic tests to detect an excessive insulin response to oral carbohydrate

An excessive insulin response to oral carbohydrate can be detected using either the oral glucose test (OGT) or the oral sugar test (OST). The OGT provides a carbohydrate bolus in the form of glucose powder mixed with chaff, whilst the OST uses carbohydrates in a commercially available corn syrup. We have demonstrated that these tests are comparable¹⁵ and measurement of peak circulating insulin concentration following a single feed of glucose¹⁶ or corn syrup¹⁷ provides a simple and practical way of identifying animals at increased risk of endocrinopathic laminitis.

Ease of administration of the sugar in syrup form and the possibility of obtaining a single blood sample post-administration make the OST an attractive option for use by veterinarians. A single dose of 0.15mL/kg bwt corn syrup (Karo Light Corn Syrup) for the OST has been used,¹⁸ but limited differing doses have been investigated. Higher doses, which provide amounts of sugar more similar to the oral glucose test, may afford improved diagnostic abilities. We have demonstrated that using a higher dose (0.45mL/kg bwt) of commercially available corn syrup (Karo Light Corn Syrup) for the OST is more reliable than the lower dose for the identification of ID and laminitis risk¹⁹ and this higher dose is now recommended by the Equine Endocrinology Group and UK equine clinical pathology laboratories.

Initial advice was to perform the OST after fasting;²⁰ however, we have demonstrated that whilst there are significant differences between fasting and fed state for area under curve insulin and serum insulin concentration 60, 75 and 90 min post administration, dichotomous interpretation for ID was similar using study identified cut-off values.¹⁷ Thus, ideally horses should be fasted for between three and 12 hours before the OST, but the test can still be performed in horses maintained at pasture.

3) Dynamic tests to detect tissue insulin resistance

The insulin tolerance test measures the glycaemic response to exogenous insulin and is currently recommended to determine tissue insulin resistance.²¹

Measuring Circulating Adiponectin Concentrations

Adipose dysregulation manifesting as abnormal plasma adipokine concentrations including hypoadiponectinemia¹⁴ and hyperleptinemia¹³ is an additional feature of EMS. Adiponectin is an adipose-derived hormone with anti-inflammatory and insulin-sensitising actions and we have demonstrated that circulating concentrations of this adipokine are lower in animals with a history of endocrinopathic laminitis²² and in healthy animals that go on to develop laminitis.¹⁴ Thus, measurement of adiponectin concentrations is recommended as an additional measure of laminitis risk.⁵ We have worked with Axiom Veterinary Laboratories in the development of a total adiponectin assay, which had been available to veterinarians since 2019.

Prevention of Endocrinopathic Laminitis

Prevention of endocrinopathic laminitis is key and relies on owners instituting a variety of management changes to ensure that the animal loses weight if they are overweight/obese or remains at an ideal weight, and to restrict carbohydrate intake to minimise the resultant insulinaemic response.

1) Weight loss tracking

Weight monitoring is a crucial element to weight management in equidae. Billions have been invested into digital healthcare start-ups and a multitude of apps have been developed to aid human weight loss. We designed a weight loss monitoring app (Equine Weight Loss Diary)



for horse owners and evaluated the owner's commitment to success with a weight loss plan for their animal. Most (66%) owners felt that a weight loss monitoring app would be helpful and the majority (80%) who used the app found it helpful (unpublished data). Thus, digital technology is available that will support owners that are trying to get their horses or ponies to lose weight.

2) Strip grazing

Strip grazing is a management technique that can be used to reduce grass intake whilst an animal is at pasture. However, there is the concern that the consequent reduction in field size will have the negative effect of a reduction in physical activity. Accelerometers are wearable sensors that have been used to quantify physical activity in humans and dogs. We have validated the use of these devices in horses and revealed that they can be used to distinguish between standing, grazing and locomoting whilst an animal is at pasture.²³ We subsequently used them to demonstrate that strip grazing does not result in reduced physical activity.²⁴ Thus, any reduction in calorie intake does not appear to be offset by a reduction in energy expenditure and so strip grazing should be an effective management tool to encourage weight loss or maintain an ideal weight in the horse.

Summary

Whilst there are still many questions relating to endocrinopathic laminitis that remain to be answered, we have demonstrated that animals at an increased risk of endocrinopathic laminitis can be identified using a high-dose oral sugar test and by measuring circulating concentrations of the adipokine adiponectin. Prevention of endocrinopathic laminitis is key and relies on owners instituting management changes to ensure that the animal loses weight if they are overweight/obese or remains at an ideal weight, and to restrict carbohydrate intake to minimise the resultant insulinaemic response. We have developed a weight loss monitoring app that will support owners that are trying to get their horses or ponies to lose weight. In addition, we have demonstrated that strip grazing does not result in a reduction in physical activity that might detrimentally offset any reduction in pasture intake.

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