Equine metabolic syndrome: *A new approach*

Sandra Forsyth, of SVS Laboratories, outlines some of the shortcomings of traditional testing protocols for EMS.

INTRODUCTION

Equine metabolic syndrome (EMS) brings to mind a fat, foundered, cresty-necked pony. However, horses may have the condition without these classical signs, necessitating laboratory testing to confirm a diagnosis. Recent studies have found that previous reference intervals may not apply to new analytical methodologies, and testing protocols that were once proposed have been re-evaluated, producing new recommendations.

PATHOGENESIS AND CLINICAL SIGNS

EMS is a condition in which insulin dysregulation (ID) causes chronically elevated serum insulin concentrations, predisposing a horse, pony or donkey to laminitis and possibly peripheral oedema, reduced fertility and abdominal lipoma development. Although well-fed, under-exercised, overweight ponies are the typical animals developing EMS, the condition can be seen in equine patients who do not carry excess weight, but who frequently show localised fat deposits over the neck and hindquarters and around the prepuce. Diets high in sugars and starches (non-structural carbohydrates) are thought to initiate insulin resistance, possibly by altering the gut microbiota (Elzinga et al., 2016). Genetics also play a role, and breeds that are 'good doers' are predisposed to the syndrome. It also appears that the condition of a mare during pregnancy can influence a foal's metabolic response later in life (Robles et al., 2018). The mechanisms by which laminitis develops as a consequence of hyperinsulinaemia are not fully established, but may include reduced blood flow, inflammation and altered cell proliferation in the lamellae.

LABORATORY DIAGNOSIS

Laboratory diagnosis of EMS hinges on finding inappropriately elevated serum insulin concentrations. Basal serum insulin concentration may be increased, although many animals with EMS do not show this, and challenge/dynamic tests can be required in order to make a diagnosis. Serum glucose and triglycerides are sometimes concurrently assessed to determine whether hyperglycaemia and/or hyperlipidaemia are also present.

FACTORS THAT MAY AFFECT LABORATORY RESULTS

Insulin and glucose may be affected by factors other than ID, and these must be minimised or accounted for during the interpretation of results. For example, acute stress and pain activate the adrenocortical axis, increasing glucose and insulin concentrations. Although it was originally recommended that fasting precede blood sampling for a basal insulin concentration, as little as six hours without feed can cause insulin resistance in horses and ponies (Bertin et al., 2016). While maintaining access to feed may mitigate this effect, the presence of ingesta in the GI tract alters gastric emptying and glucose/dextrose transit during challenge testing, thereby altering peak serum glucose and insulin concentrations. The current recommendation when assessing basal insulin is to allow horses access to grass or hay, and to avoid haylage and grain that could increase insulin concentrations to equivocal levels. Fasting is still recommended during a glucose challenge test (Durham et al., 2019).

INSULIN ASSAYS

Diagnosing ID requires an accurate determination of the serum insulin

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concentration. Equine insulin can be assessed in the laboratory by various methods, including enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (RIA) and chemiluminescence. These methods have statistically significant differences between the determined insulin concentrations (Warnken et al., 2016). Early studies using RIA and on which reference intervals in most laboratories are based found that basal insulin concentrations over 20μIU/mL (139pmol/L) suggested ID. Using this cut-off point, horses with ID may be misclassified as having normal insulin sensitivity when analysis is via chemiluminescence because insulin concentrations tend to be lower than those provided by RIA and ELISA for concentrations under 100μIU/ml (694.5pmol/L) (Warnken et al., 2016; Carslake et al., 2017). Thus, results just under the cut-off using chemiluminescence methodology should be treated as suspicious or equivocal.

GENETICS PLAY A ROLE, AND BREEDS THAT ARE 'GOOD DOERS' ARE PREDISPOSED TO THE SYNDROME.

DYNAMIC TESTING

Dynamic (challenge) testing is carried out in animals who are suspected of having EMS but who have normal or equivocal resting insulin concentrations. Glucose or dextrose is administered orally or by IV injection, and the response to the sugar load is monitored and compared to results seen in normal animals.

Numerous protocols for dynamic testing are reported in the literature, several of which are too complicated or expensive for routine diagnostic use. Oral glucose tests (OGTs) are relatively common and are performed by providing a sugar source mixed in a meal. The most frequently assessed protocols administer corn syrup (Karo Light Syrup), which is not currently available in New Zealand. Alternative protocols include oral glucose or dextrose powder mixed in a small amount of feed. These may be unpalatable, and prior overnight fasting is recommended to improve compliance in eating the meal. Fasting also standardises gastric emptying. One of the more common protocols is to collect serum two hours after feeding the horse/pony 1g/kg of glucose/dextrose. The measured serum insulin concentration that reflects ID is >80μIU/mL (555.6pmol/L), using the IMMULITE 1000 chemiluminescent analyser (Durham et al., 2019). Glucose or dextrose may be administered by nasogastic tube, provided that sedation and associated stress are avoided.

GLUCOSE AND TRIGLYCERIDES

The majority of horses with EMS are not hyperglycaemic. However, occasional cases of diabetes mellitus are detected.

Lipid abnormalities are commonly present in animals with EMS, and elevated triglyceride concentrations may be a predictor of laminitis. Yet despite statistically significant differences between healthy and affected horses, changes are generally too small to be detected clinically. That said, it is recommended that serum triglyceride concentration be monitored to detect hyperlipidaemia and a negative energy balance in horses undergoing treatment for EMS, particularly pregnant animals, miniature horses and Shetland ponies (Durham et al., 2019).

MONITORING

Monitoring of insulin concentration is recommended to confirm that a reduction in insulin resistance is occurring as a result of the recommended therapeutic interventions. While a challenge test is most reliable, assessing serum insulin concentration two hours after the morning feed or two hours after turning out onto pasture is adequate. Horses over the age of 10 who are investigated for ID should also have adrenocorticotropic hormone (ACTH) concentrations assessed because laminitis is also associated with pituitary pars intermedia dysfunction, which often coexists with ID.

SUMMARY

EMS is not uncommonly encountered, and while baseline insulin may provide a diagnosis in some animals, glucose challenge tests may be required in others. Recent studies have found that previous protocols such as fasting for baseline testing are no longer recommended, and the changing methodology for insulin assessment necessitates care when interpreting results. (VS)

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