IN FOCUS

Investigating equine endocrinopathies

What are the options for treating pituitary pars intermedia dysfunction and equine metabolic syndrome?

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Equine pituitary pars intermedia dysfunction (PPID) is a slowly progressive neurodegenerative disease with a loss of dopaminergic (inhibitory) input to the melanotropes of the pituitary pars intermedia (McFarlane, 2014). It appears to be associated with localised oxidative stress and abnormal protein (a-synuclein) accumulation, but the exact cause remains unknown. The consequent dysfunction of the region results in hyperplasia of this area of the gland and overproduction of normal pars intermedia-derived hormones. Eventually the area undergoes adenomatous change.

The condition is seen in older animals; the average age in retrospective case series ranges from 18 to 23 years. There is no breed or sex predilection, but ponies appear to be more frequently affected than horses. The clinical signs can be roughly divided into those that are seen early in the disease and those that are associated with advanced disease.

Early signs include decreased athletic performance, change in attitude/lethargy, delayed hair coat shedding, regional hypertrichosis, change in body conformation, regional adiposity and laminitis. Late signs include lethargy, generalised hypertrichosis (Figure 1), skeletal muscle atrophy (Figure 2), hyperhidrosis, polyuria/polydipsia, recurrent infections, infertility and laminitis. There is no ideal further diagnostic test for equine PPID, but plasma basal adrenocorticotropic hormone (ACTH) concentrations and the ACTH response to TRH are currently thought to be the most appropriate tests available. In addition, since a subset of animals with PPID have insulin dysregulation (ID), tests to detect ID should be undertaken.

Equine metabolic syndrome (EMS) is a collection of risk factors for endocrinopathic laminitis (Durham et al., 2019). The central and consistent feature of EMS is insulin dysregulation which can manifest in three ways, namely: hyperinsulinaemia, an excessive insulin response to oral carbohydrate and peripheral (tissue) insulin resistance. Additional features of EMS include obesity (Figure 3), hypertriglyceridaemia and adipose dysregulation manifesting as abnormal plasma adipokine concentrations including hypoadiponectinaemia and hyperleptinaemia. Laminitis is the primary clinical consequence of EMS (Figure 4). Horses with EMS might also be at risk of further problems including hyperlipaemia and critical care-associated metabolic derangements including hyperglycaemia and hypertriglyceridaemia. A diagnosis of EMS is based on demonstration of ID. Resting (basal) insulin concentrations can be measured to detect hyperinsulinaemia, but this is of low diagnostic sensitivity. Ideally, dynamic tests should be performed including an oral sugar test (OST) to detect an excessive insulin response to oral carbohydrate and an insulin tolerance test (ITT) to assess tissue insulin sensitivity.

Treatment of PPID

Seeing as PPID is a slowly progressive, lifelong condition, the aim of treatment is to improve the quality of life through reducing the clinical signs, rather than cure the condition. Whilst the benefits of treating an animal with PPID that has life-threatening clinical signs such as laminitis are clear, the decision to specifically treat the PPID in animals with clinical signs that are not life threatening is less clear-cut.

There is no published evidence demonstrating that pergolide prevents laminitis or the progression of PPID. It could be argued that pharmacological management in such cases is appropriate, as it should be considered to be prophylactic treatment of a condition that may threaten health in the future. Thus, this decision should be made following discussion with the owner taking into account the financial implications and potential adverse effects of life-long treatment.

Pharmacological treatment

There are two types of drug available: dopamine agonists and serotonin (5-hydroxytryptamine; 5-HT) antagonists. The former replace the lost dopaminergic inhibition to the pars intermedia, whilst the latter decrease the serotonin-induced stimulation to the pars intermedia. Both result in a reduction in the excessive hormone secretion and so an improvement in the clinical signs. It has not been determined whether treatment with these drugs also inhibits the development/progression of the pituitary hyperplasia or reduces the size of pituitary adenomas once they have developed.