**Getting the old guys back on track: Management of PPID**

Professor Catherine McGowan

The University of Liverpool

Dept. Equine Clinical Science, Institute of Veterinary Science

Leahurst campus, Neston, CH64 7TE

*Treatment, monitoring and management of PPID including nutritional management and considerations for the geriatric horse.*

**Introduction**

With the licensing and marketing of pergolide (Prascend) medical treatment for equine pituitary pars intermedia dysfunction (PPID or Equine Cushing’s disease) has become more common. Unlike the case a decade ago where conservative management was sometimes still advocated, medical treatment of PPID is now the accepted ‘norm’ and owners should be fully informed about the treatment options. However, medical treatment is just the first step and the key to success in these old guys is monitoring and follow-up. This needs to be done in the context of geriatric horse health and welfare, but if well managed, these cases and their owners are an important part of equine practices.

The aims of this presentation are to:

1. Outline the treatment of PPID and how it works, including side effects and dose adjustment and prognosis.
2. Outline the benefits and method for monitoring PPID cases on treatment with endocrinological testing and owner participation in monitoring clinical signs.
3. Discuss how to manage the difficult case, including cases with concurrent diseases associated with older age, concurrent equine metabolic syndrome or laminitis and nutritional management.

**Treatment**

Before treatment is started, it is important to ensure horse owners are aware of the disease and understand its basic pathophysiology and how the treatment works. A comparison with Parkinson’s disease in humans or ‘accelerated aging’ is often the best way to explain it, rather than talking about tumours in the pituitary (see also Equine Cushing’s Disease/PPID – what do we know now?). Similarly, likening the sleepy dull appearance of a PPID horse to the high circulating opiates (β-endorphin) and seeing the improvement in demeanour with treatment can help an owner understand their horses’ quality of life.

Medical treatment of PPID involves Pergolide, (Prascend, Boehringer Inghelheim) a dopamine agonist, which is licensed for use at a dose from 0.002 – 0.01 mg/kg PO q24h. Treatment should be initiated at the low end of the dose range (to the nearest 0.5 mg) and gradually increased, if required, based on clinical and endocrinological response. 1

|  |  |
| --- | --- |
| Body Weight | Starting Daily Dose |
| 200-350 kg | 0.5 mg |
| 350-600 kg | 1.0 mg |
| 601-850 kg | 1.5 mg |

**Side effects**

Some horses will become inappetant on pergolide, and some may appear dull. This side effect was more common when pergolide was first used at much higher initial doses and as such can typically be avoided by reducing the dose for that animal.

If signs of inappetance or depression are observed, reduce the dose by increments of 0.001 mg/kg BW or stop treatment for a short period (2-3 days or till appetite returns) and the dose restarted at half of the original dose. 1 It may also be pertinent to investigate for concurrent disease as discussed below.

The side effects observed in affected horses are not reported in normal horses. Pergolide administered at doses as high as 0.008 mg/kg for 6 months in target animal safety studies did not induce observable depression or anorexia. 2 There were decreases in heart rate variably between geldings and mares, but only to the normal range. Further research using normal horses in a blinded controlled cross over design trial using more detailed heart rate observations using holter monitor recording at rest, during stimulation and exercise did not demonstrate a difference in heart rate between groups. 3

**Monitoring**

Owners should be made aware that treatment is life long and that regular monitoring of their horse along with treatment will allow for the best outcome. It is important to remember that no treatment for PPID can actually reverse the pathology that is occurring so specific monitoring is essential. Monitoring of clinical signs, basal ACTH concentration and insulin dysregulation will provide the best information.

*General health monitoring*: Although PPID is associated with a range of clinical signs including hypertrichosis, muscle wasting, and laminitis, many signs that occur in PPID horses are not more prevalent than other horses of a similar age. Most horses with PPID will be in their ‘teens’ or older, with an increasing likelihood of diagnosis every year after 15 years of age. 4 Aged and geriatric horses have an increased susceptibility to a range of conditions and diseases even without PPID. These are particularly dental disease, lameness, eye conditions, heart or lung conditions and skin conditions (see also Equine Cushing’s Disease/PPID – what do we know now?). PPID will increase the risk of intestinal parasitism 5 but does not alter a routine haematological or biochemical profile 4 so apparent alterations in blood tests and illnesses should be investigated as concurrent disease, not ignored as part of PPID. In aged horses with PPID, there is a higher possibility of serious dental problems as well as peridontitis, so dental work should be carried out with due veterinary care including sedation, pain relief and anti-inflammatory or other medication as necessary. If owners are fully informed of the high prevalence of these conditions in their horses’ age bracket, and engage in regular health checks with appropriate blood testing, then the best outcomes can be achieved.

*Monitoring clinical signs*: Body condition score (and muscle score), hair coat, demeanour, appetite, Obel grade of lameness if lame (or the evidence of subclinical laminitis like laminitic rings, widened white line or dropped soles if not) and water intake can all be monitored. Owners can be encouraged to monitor and record these e.g. monthly.

Endocrine monitoring should include both monitoring of PPID as well as monitoring for the risk of laminitis.

*PPID endocrine monitoring:* The first follow up for a horse starting treatment for PPID should be within 4-6 weeks. 1 At this time basal ACTH should have decreased substantially (by at least 50%) or be within the normal reference range, bearing in mind the seasonal increase in ACTH from late summer. One or more clinical signs should have also improved, with the earliest reported improvements often in the horse’s demeanour. Other clinical signs may take several months. If clinical and/or endocrine improvements are not noted, increase the dose of pergolide by 0.001 mg/kg BW/day. Each increment in dose should be followed up similarly (within 1-2 months) until the horse stabilises. If clinical signs have stabilised for more than 3 months on > 0.002mg/kg/day pergolide, a decrease of the pergoide dose by 0.001 mg/kg BW/day to not less than 0.002mg/kg/day can be attempted. Each increment down in dose should be followed up similarly (within 1-2 months). 1

Once a suitable dose has been determined, follow up monitoring can decrease to one or two times a year. If possible, it may be useful to include at least one follow up test a year during the autumn when there is peak ACTH and maximal ACTH activity.

*Monitoring for the risk of laminitis:* In addition to monitoring PPID, it is also worthwhile measuring insulin dysregulation, either basally or dynamically. Horses with PPID are more likely to be hyperinsulinaemic and develop laminitis than aged matched controls. Although only just over a third of horses with PPID are likely to be insulin dysregulated, 4 insulin is an important prognostic indicator for PPID survival overall and the degree of insulin dysregulation provides a good indication of the risk of laminitis. 6,7

*Dietary considerations:* Many horses with PPID are underweight and dietary considerations focus on minimising muscle loss and ensuring they can eat what is offered. Careful attention to protein (especially high quality amino acid supplementation) and vitamin and mineral supplementation is important to prevent and reverse muscle loss and atrophy. 8 In horses with more marked weight loss or unable to cope with long fibre, for example, due to dental disease, low glycaemic short fibre (chaff based) or complete rations can be purchased. Higher fat rations provide a high density caloric source and tend to induce lower insulinaemic responses when fed.

In horses with PPID and insulin dysregulation, dietary restriction to reduce the risk or consequences of laminitis may be considered. However, horses with PPID are already at risk for muscle atrophy as a result of muscle catabolism 8 so dietary consideration should focus on the insulinaemic response to feeds rather than on management of obesity and weight loss (see Back on their feet again: Management of endocrine laminitis). Even in obese PPID affected horses, weight loss should be carefully monitored and slower, carefully monitored reductions of bodyweight aimed for than in younger horses with equine metabolic syndrome.

**Prognosis**

As mentioned above, there is now good evidence to suggest at least 75% of treated horses should respond to therapy, including advanced cases2 and long term improvements over many years have been maintained. 9 Less advanced cases (and some advanced ones) can return to athletic function and even competition, although competing on pergolide is still not allowed in many events so this should be checked before competition.

Prognosis is better in horses with controlled insulin dysregulation, even if this is unable to be completely normalised. 6 However, some advanced cases of PPID with insulin dysregulation can prove difficult to manage, even in the face of normalisation of ACTH concentrations. In these cases management of the insulin dysregulation using careful dietary control is advised. As mentioned in the talk on endocrinopathic laminitis, it is the carbohydrate content of the diet that creates the hyperinsulinaemia, so rather than focussing on weight loss, management of the PPID horse should focus on reducing the carbohydrate content of the diet, including (and especially) the forage component. In some cases metformin may help. 1 Excessive weight loss in the PPID case can exacerbate catabolism and be difficult to reverse. Similarly, careful attention to protein (especially high quality amino acid supplementation) and vitamin and mineral supplementation is important to prevent and reverse muscle loss and atrophy.

**References**

1. Durham AE, McGowan CM, Fey K, Tamzali Y, Kolk, JH. Pituitary pars intermedia dysfunction: diagnosis and treatment. *Equine vet educ.* 2014; 26, 216-223.
2. NADA (2011) Freedom of Information Summary – Prascend tablets for the control of clinical signs associated with pituitary pars intermedia dysfunction (equine Cushing’s disease) in horses. Available at: <http://www.fda.gov/downloads/AnimalVeterinary/Products/ApprovedAnimalDrugProducts/FOIADrugSummaries/UCM280354.pdf>.
3. McGowan CM, Dugdale AH, Ireland JL, and Argo CMcG. Effect of pergolide on heart rate and behavioural responses to a novel object. European Equine Endocrinology Symposium, 2014; Windsor UK pp. 44-45.
4. McGowan TW, Pinchbeck GP, McGowan CM. Prevalence, risk factors and clinical signs predictive for equine pituitary pars intermedia dysfunction in aged horses. *Equine vet. J*. 2013; 45(1):74-9.
5. McFarlane D, Hale GM, Johnson EM, Maxwell LK. Fecal egg counts after anthelmintic administration to aged horses and horses with pituitary pars intermedia dysfunction. *J Am Vet Med Assoc*. 2010;236(3):330-4.
6. McGowan CM, Frost R, Pfeiffer DU and Neiger R. Serum insulin concentrations in horses with equine Cushing's syndrome: response to a cortisol inhibitor and prognostic value. *Equine vet J.* 2004; 36: 295-298.
7. Karikoski NP, Patterson‐Kane JC, Singer ER, McFarlane D, McGowan CM. Lamellar pathology in horses with pituitary pars intermedia dysfunction. *Equine vet J.* 2016; 48(4):472-8.
8. Aleman M, Watson JL, Williams DC, LeCouteur RA, Nieto JE, Shelton GD. Myopathy in horses with pituitary pars intermedia dysfunction (Cushing’s disease). *Neuromuscul Disord*. 2006; 16(11):737-44.
9. Schott, H.C. 2nd (2006) Pituitary pars intermedia dysfunction: challenges of diagnosis and treatment. In: *Proc Ann Conv AAEP* 2006. pp60-73.