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THE POTENTIAL USEFULNESS AND APPLICATIONS OF ADIPONECTIN TESTING IN HORSES WITH SUSPECTED EMS

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Background

The best studied adipokines in horses comprise adiponectin and leptin. Particular focus has been placed on adiponectin as this appears to be one of the most highly expressed adipokines and is better associated with the functional adverse health consequences of obesity rather than simply reflecting the physical mass of adipose tissue. Adiponectin is a 244 aminoacid protein produced almost exclusively by adipocytes and is structurally similar to inflammatory proteins such as complement factor C1q and TNF-alpha. The effects of adiponectin include anti-inflammatory actions, decreasing vascular tone and increasing insulin sensitivity. In the circulation adiponectin tends to form trimers, hexamers or HMW multimers consisting of 4 to 6 trimers. ***The HMW forms of adiponectin appear to be most biologically active and correlate best with insulin sensitivity.***

In a recent Australian study[1] comparing overfeeding horses and ponies, only those fed high starch diets became insulin dysregulated whereas those that became fat on high oil diets did not. Leptin was found to be abnormal in both groups (simply reflecting fat mass) whereas adiponectin values only became abnormal in the high-starch, insulin dysregulated group indicating a better association with the metabolic effects of obesity.

Adiponectin values are abnormally *decreased* in obesity. Obesity not only suppresses adiponectin secretion but also decreases the relative presence of the more biologically active HMW forms. Hyperinsulinaemia also suppresses adiponectin receptor expression and may lead to “adiponectin resistance”.

In some other species females tend to have higher HMW adiponectin concentrations than males (as testosterone decreases adiponectin secretion) although geldings appear to have similar levels to mares. Some studies indicate that exercise and aerobic fitness promotes adiponectin production also. Adiponectin is stable when chilled but does show some decrease in values after 24 hours *in vitro* at >20°C. There is no circadian pattern in horses and adiponectin is not notably affected in response to feeding or exercise.

Summary of recent clinical studies

In a study conducted in the UK[2], a large group of mature to elderly ponies were selected that had never previously had laminitis and did not have PPID. Several blood tests were performed and subsequent laminitis status monitored. Within 2 years of testing, 30 ponies (7%) had suffered laminitis attacks. Total adiponectin concentration and basal insulin were the only 2 simple blood tests that were able to predict laminitis in this group. Of the 30 ponies that developed laminitis within 2 years, 24 (80%) had abnormally low total adiponectin values compared to only 20% of those that remained non-laminitic. In this population of mature to elderly, never previously laminitic ponies, a high total adiponectin concentration was quite reassuring and indicated a low risk of laminitis. Laminitis was >10 times more likely to occur within 2 years in those with low adiponectin, although many such individuals did not go on to develop laminitis.

Thus we should not expect that low adiponectin is always associated with EMS and laminitis risk, but high adiponectin offers some reassurance and low adiponectin indicates significantly increased risk.

In a German study[3], a group of mature ponies were subject to a weight loss programme by feeding limited hay for 14 weeks. Total adiponectin concentrations were found to be significantly correlated with the insulin sensitivity of the ponies (i.e. low adiponectin = low insulin sensitivity). Approximately 14% body mass was lost during the study and this was associated with significant increases in total adiponectin suggesting that ***the test may be useful for supporting weight loss programmes***.

Both of the studies mentioned above measured total adiponectin but only one[4] has looked at HMW adiponectin in horses. Mean HMW adiponectin was shown to be significantly higher in lean than obese horses (8.0 ± 4.6 vs 3.6 ± 3.9 ug/mL). HMW adiponectin in lean horses ranged from 2.8-24.2 ug/mL versus 0.7-4.9 ug/mL in obese horses. Gender and age did not affect HMW APN.

Clinical Comment

Time and further clinical experience will tell how useful measurement of adiponectin will be in diagnosing and managing EMS cases. However, there would appear to be 3 main potential advantages to consider:

1. **Endocrinopathic laminitis diagnosis and monitoring**

Oral sugar tests (Dextrose or Karo Light Corn Syrup) are popular and practical for use in general practice to indicate insulin dysregulation as seen in EMS and PPID. However, although useful for an indication of pasture associated laminitis risk, these tests do not always improve well in association with weight loss and therefore are often not encouraging for owners committed to an effective weight control programme. Although this author prefers intravenous tests for insulin sensitivity when assessing weight loss programmes (eg. combined insulin glucose test or the insulin tolerance test) such intravenous tests are unpopular in practice and it would be useful to have another simple test to help monitor and encourage weight loss (or weight gain). Studies such as those mentioned above[1,3] establish ***a reasonable basis for adiponectin as part of weight monitoring*** although only time will tell how useful adiponectin is in clinical practice in this respect.

2. **Combination PPID-EMS cases**

Clearly PPID and EMS may coexist but, after making a diagnosis of PPID it is hard then to support a diagnosis of EMS in addition and help emphasise the importance of weight loss in these cases. Clearly all tests for insulin dysregulation (Oral sugar test, CGIT, ITT etc…) will be abnormal in both PPID and EMS. However, ***adiponectin may offer us a test that is additionally supportive of EMS in PPID cases*** and the need for weight control in these combination cases, rather than simply treating them with pergolide.

The Liphook Equine Hospital has always been committed to providing the latest state of the art, evidence-based tests for use in practice. We will be very interested to see how useful our HMW adiponectin assay proves to be in clinical practice and rest assured that we will feedback our findings (good and bad) as this becomes more apparent.

References

[1]**Bamford** *et al.* 2016 Effect of increased adiposity on insulin sensitivity and adipokine concentrations in different equine breeds adapted to cereal-rich or fat-rich meals. Vet J.;214:14-20.
[2]**Menzies-Gow** *et al.* 2016 Prospective cohort study evaluating risk factors for the development of pasture-associated laminitis in the United Kingdom. Equine Vet J. (epub ahead of print)
[3]**Ungru** *et al.* 2012 Effects of body weight reduction on blood adipokines and subcutaneous adipose tissue adipokine mRNA expression profiles in obese ponies. Vet Rec.;171(21):528.
[4]**Wooldridge** *et al.* 2012 Evaluation of high-molecular weight adiponectin in horses. Am J Vet Res. 73(8):1230-40.