Diagnosis and Management of Insulin Resistance and Equine Metabolic Syndrome (EMS) in Horses

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Introduction

The term 'equine metabolic syndrome (EMS)' has been adopted to describe a collection of clinical signs that contribute to the development of founder (laminitis) in horses. Equine metabolic syndrome has not been rigorously defined and critics rightfully argue that more studies are required to substantiate its existence. However, it is still useful to recognize this clinical syndrome because horses and ponies with EMS are at greater risk for developing laminitis, and effective management of this condition appears to aid in the prevention of this disease.

Definition

This syndrome is currently defined by the presence of 1) insulin resistance (IR), 2) obesity and/or regional adiposity, and 3) prior or current laminitis. Insulin resistance is a disturbance of glucose metabolism that can be thought of as an early form of type 2 diabetes mellitus. In humans, type 2 diabetes is more common in obese individuals and high-sugar diets make the situation worse. This disease differs from type 1 (juvenile) diabetes, which occurs when the pancreas cannot secrete enough insulin to regulate blood glucose levels after eating. People with type 1 diabetes mellitus must inject themselves with insulin to regulate their blood sugar.

Diabetes is extremely rare in horses, but IR is much more common and this condition is important because of its association with laminitis.[1,2] In the majority of cases, horses compensate for IR by increasing insulin secretion from the pancreas. Your veterinarian may suggest checking your horse's blood insulin level because a very high concentration is diagnostic for IR in horses and ponies. Episodes of laminitis are triggered by grazing on lush grass (pasture-associated laminitis or grass founder) or can occur spontaneously without an identifiable cause. Horses sometimes suffer from mild laminitis episodes that go unnoticed. These horses may develop prominent growth rings on the hooves that are narrower at the front than at the heels (founder lines). Other horses show only mild lameness, but rotation of the pedal bone is seen when x-rays are taken of the feet.

One key feature of EMS is that affected horses are often described as 'easy keepers' because they seem to require fewer calories to maintain body weight. As a result, these horses are obese or exhibit regional adiposity. The latter term refers to the accumulation of fat tissue in abnormal locations. Presence of a 'cresty neck' is the most important form of regional adiposity in horses, but noticeable fat deposits are sometimes found close to the tailhead, in the sheath, above the eyes, and occasionally as bumps along the sides of the horse.

Obesity and laminitis have also been attributed to hypothyroidism in the past, but we now recognize that low thyroid hormone concentrations are detected in horses with a

variety of medical conditions,[3] and hypothyroidism can only be diagnosed by performing a hormone challenge. When low resting thyroid hormone concentrations are detected in obese insulin resistant horses, they are more likely to be a consequence rather than the cause of the problems seen.

Clinical presentation

Based upon our experience, EMS is most common in pony breeds, Morgans, Paso Finos, and Norwegian Fjords. We have also examined Arabians, Quarter Horses, Saddlebreds, Tennessee Walking Horses, Thoroughbreds, and Warmbloods with this condition, indicating that a number of breed groups are represented.[4] When viewed simplistically, easy keeper breeds are most commonly affected, whereas hard keeper breeds such as Thoroughbreds and Standardbreds are less likely to develop EMS.

Susceptibility to EMS is likely to be established from birth and some horses develop obesity at 3 or 4 years of age. However, most horses are between 5 and 15 years of age when veterinary or farrier services are first required because of laminitis. Many horses are out on pasture when laminitis is first detected, and this occurs more frequently in the spring when the pasture has gone through a period of rapid growth. Obesity has also been associated with abnormal reproductive cycling in mares.[5]

Testing procedures

Resting serum insulin concentrations

This is the easiest measurement to perform and is a useful screening test because high serum insulin concentrations are detected in horses and ponies with moderate to severe IR. Blood samples must be collected from horses after they have been held off pasture for at least 12 hours and fed hay overnight. Grazing on pasture can raise serum insulin concentrations if the sugar levels are high in the grass, and grain will cause a peak in insulin levels for a few hours after a meal has been consumed. Your veterinarian should use the reference range for their laboratory because there is some variation between laboratories. At the University of Tennessee, the upper limit of the insulin reference range is 30 μU/mL (mU/L), but we consider > 20 μU/mL to be suggestive of IR. High-normal glucose concentrations (> 100 mg/dL or 5.5 mmol/L; multiply by 18 to convert units) are also detected in some horses with IR.

Pain and stress associated with acute laminitis markedly elevate resting serum insulin concentrations in EMS patients. Resting serum insulin concentrations can often range from 100 to 400 μU/mL in horses and ponies with clinical laminitis. It is therefore necessary to reevaluate these patients several weeks later after the pain of laminitis has subsided.

Combined glucose-insulin test (CGIT)

This dynamic test provides a better estimation of insulin sensitivity and can detect IR in patients with mild IR. Your veterinarian can contact the author to obtain more information about this test. Horses must be held off pasture and fed only hay the night before testing. Hay can also be fed free choice during the test and this will help to keep the horse calm during the procedure. The intravenous catheter should ideally be placed

the night before testing to minimize the confounding effects of stress, but quieter horses can be tested on the same day. The test takes approximately one hour to perform.

Dietary management of insulin resistance in horses

Two important questions must be addressed before selecting a feed for an insulin resistant horse – is the feed likely to make the IR worse and will it increase the risk of laminitis?

Inducing weight loss in obese insulin resistant horses

Individual horses should be fed according to their metabolic needs. Obese horses that are easy keepers can be placed on a simple diet of hay and a vitamin/mineral supplement. Concentrates are not necessary for these obese horses and weight loss should be promoted by restricting the horse's caloric intake until its ideal weight and body condition have been achieved. This ideal set point differs between individual horses and breeds because the physical stature of the animal varies considerably. The horse must be taken out of its obese state, but it is not necessary for every horse to assume an underweight condition.

Weight loss strategies include dietary management and exercise. Obese horses should be fed enough hay to meet their energy needs, which is usually equivalent to 1.5 to 2.0 % of body weight (15 to 20 lbs hay for a 1000-lb horse). Clients should be asked to weigh their hay so that the correct amount is fed. Hay with a low (< 12%) non-structural carbohydrate (NSC) content should be selected for obese insulin resistant horses. Non-structural carbohydrates include simple sugars, starch, and fructans, but NSC measurements reported by commercial laboratories may only include simple sugars (ethanol-extracted soluble carbohydrates) and starches. If the NSC content exceeds 12%, soaking it in cold water for 30 minutes will lower the sugar content prior to feeding. Grass or alfalfa hay can be fed as long as NSC content has been measured. Forages can also be purchased from commercial sources if clients have difficulty acquiring low-NSC hay. Complete feeds and bagged forages are available for insulin resistant horses.

Horses should also receive 1,000 IU vitamin E per day as a supplement because access to green grass has often been restricted. A protein supplement may also be necessary if the quality of hay is poor. Patients that are laminitic should not be exercised until hoof structures have stabilized, but unaffected horses should be exercised regularly. Ideally, horses with EMS should be walked on a lead rope, exercised on a lunge line, or ridden every day.

Avoiding feeds that exacerbate IR

In addition to exercise, care must be taken to avoid feeds that exacerbate IR. The horse with EMS is similar to a person with diabetes, so excessive sugar should be avoided. Treats containing sugar and sweet feeds should be eliminated from the diet. Unfortunately, it is very difficult to control sugar intake when horses are grazing freely on pasture. Pasture grass is one of the largest sources of sugar in the horse's diet and the carbohydrate content varies between regions and depends upon soil type, climate, hours of sunlight, and grass species. It also varies according to season and time of day, which causes fluctuations in sugar intake that can make IR worse and possibly trigger an

episode of laminitis. Access to pasture must therefore be restricted or eliminated when managing insulin resistant horses and ponies. Sometimes this is only necessary for a few months until weight loss is achieved. However, there are some insulin resistant horses that must be permanently housed in dirt paddocks because they are extremely sensitive to changes in pasture grass nutrient content. Thankfully most horses and ponies with EMS can be managed by limiting grazing time to 1 to 2 hours per day, housing in a grass paddock, strip grazing using an electric fence, or application of a grazing muzzle.

Feeding more calories without exacerbating IR

Some insulin resistant horses have a leaner overall body condition, but still exhibit regional adiposity. These horses may be older and suffer from equine Cushing's disease. Other horses may be exercising strenuously or competing, so they require more calories. If hay is not sufficient to provide these calories, a concentrate must be selected.

Thin insulin resistant horses can be fed concentrates, but care must be taken to provide calories without exacerbating IR. There are three considerations when evaluating feeds for insulin resistant patients: 1) the sugar content of the feed, 2) the glycemic response after feeding (how high the blood glucose levels go after eating), and 3) feeding practices. Feeds containing less starch and sugar are appropriate in these situations. It is also advisable to feed hay before concentrates and to feed smaller meals more frequently. Feeding strategies include:

1. A diet consisting of hay with a low (< 12%) NSC content, pelleted specialty feed for IR horses, vitamin and mineral supplement, and 0.5 cup (equal to 125 mL; contains approximately 100g fat) rice bran oil or corn oil twice daily.
2. The same diet with molasses-free beet pulp substituted for pelleted specialty feed.
3. Either of the above diets with rice bran substituted for oil. Rice bran contains approximately 20% fat and 1 lb (approximately 90 g fat) can be fed twice daily.
4. A pelleted specialty feed for geriatric horses in older patients with muscle loss or dental problems (> 20 years of age).

Horses with poorer appetites sometimes refuse to eat beet pulp or specialty feeds, so a small amount of oats may be added to help with this transition. Beet pulp is energy-dense, so it is not an appropriate feed for obese horses, other than as a treat (0.5 cup) to aid in the delivery of supplements. It should be soaked prior to feeding to remove molasses and simple sugars, and lower the risk of esophageal obstruction. Even molasses-free beet pulp can contain simple sugars, so feed analysis results should be provided by the supplier prior to purchase.

Lowering the risk of laminitis

Pasture access is the most important issue when managing EMS. As mentioned previously, there are some horses that are extremely sensitive to alterations in pasture grass composition that must be permanently held off pasture. If your horse has suffered from repeated episodes of laminitis and requires special farrier care, it should be permanently housed in a dirt paddock. However, other horses have stabilized after

implementation of recommended weight loss, diet, and exercise programs. These patients can return to limited grazing on pasture. This usually begins with 1 to 2 hours of grazing once or twice a day or limited turnout with a grazing muzzle.

Basic guidelines for lowering the risk of pasture-associated laminitis include avoiding times when the grass is 1) turning green and growing quickly (spring), 2) first beginning to dry out at the start of a summer drought, 3) rapidly growing after a heavy summer rain, and 4) entering winter dormancy in the fall. In general, the insulin resistant horse or pony should be kept off pasture when the grass is in a dynamic phase. You should pay attention to your lawn and hold your horse off pasture when more frequent mowing is required.

Treatment of obesity and insulin resistance with levothyroxine sodium

Most horses or ponies with EMS can be effectively managed by controlling the diet, instituting an exercise program, and limiting or eliminating access to pasture. However, there are times when these strategies will not improve the situation fast enough to prevent additional episodes of laminitis. In these situations, drug therapy is warranted to lower the likelihood of subsequent laminitis episodes and permanent damage to the feet. If this is the case, talk to your veterinarian about treating your horse with levothyroxine sodium (Thyro L®, Vet-A-Mix, Division of Lloyd, Inc., Shenandoah, Iowa) at a high dosage to accelerate weight loss and improve insulin sensitivity. This drug should only be administered under the direction of a veterinarian and the high dosage should only be used for 3 to 6 months. Ask your veterinarian to contact the author for further information.

We have performed three research studies to evaluate the use of levothyroxine sodium (Thyro L®, Vet-A-Mix, Division of Lloyd, Inc., Shenandoah, Iowa) in horses. In our first study, we administered levothyroxine to eight mares according to an incrementally increasing dosing regimen over an 8-week period.[6] Mean body weight decreased and insulin sensitivity increased in treated mares. Our second study evaluated the long-term effects of the drug on body weight and insulin sensitivity in six mares over a 12-month period. Heart evaluations were performed and blood samples were analyzed to assess internal organs (kidney, liver, and muscle) for changes in function or damage. Advanced glucose-insulin tolerance tests were also performed at 0, 4, 8, and 12 months. Mean (± standard deviation) weight loss was 49 ± 14 kg, 43 ± 7 kg, and 25 ± 18 kg at 4, 8, and 12 months, respectively. This alteration was mirrored by a > 2-fold increase in mean insulin sensitivity. No adverse health effects were detected.

In our final study, we are examining the effects of levothyroxine on body weight and insulin sensitivity in horses affected by EMS, and this study is ongoing. Preliminary results indicate that EMS treated with levothyroxine sodium (Thyro L®, Vet-A-Mix, Division of Lloyd, Inc., Shenandoah, Iowa) lose more weight and show a greater reduction in neck circumference. Horses (n = 4) on a controlled diet exhibited a 5 cm decrease in mean neck circumference over 6 months, whereas the same measurement decreased by 10 cm in treated horses (n = 4). We have also observed that the cresty neck becomes softer in treated horses and this finding precedes the reduction in neck circumference.

Measured serum total thyroxine concentrations are elevated during treatment when the high levothyroxine sodium dosage is used, but concentrations vary widely within and between horses. Serum total thyroxine concentrations usually range from 40 to 100 ng/mL when the higher dosage is being administered, but clinical signs of hyperthyroidism such as sweating or tachycardia have not been observed in treated horses.[6-8]

When levothyroxine treatment is discontinued, horses should be weaned off the drug over a minimum of 4 weeks. We have not examined the benefits of treating horses with levothyroxine sodium at lower dosages for longer periods of time.

Conclusions

Obesity and insulin resistance are important predisposing factors for laminitis in horses and ponies. Diet changes and exercise are key components of any management plan for horses with EMS, and restricted access to pasture is the key to success when trying to induce weight loss. Levothyroxine sodium (Thyro L®, Vet-A-Mix, Division of Lloyd, Inc., Shenandoah, Iowa) can be used to accelerate weight loss and improve insulin sensitivity when the horse is threatened by laminitis. Weight loss occurs more rapidly when horses are placed on a controlled diet throughout the period of time that levothyroxine sodium is being administered.

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