Tying-Up in Quarter Horses and Thoroughbreds: Separate Diseases with Common Clinical Signs

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Although horses share similar clinical signs of acute rhabdomyolysis, numerous etiologies exist for tying-up. In Quarter Horses tying-up is often caused by a heritable glycogen-storage disorder called polysaccharide storage myopathy that can be managed by a fat-supplemented, hay-based diet, and regular daily exercise. In Thoroughbreds recurrent exertional rhabdomyolysis (RER) is often due to a heritable disorder of muscle contractility that is intermittently expressed during stress and excitement. RER is best managed by decreasing excitement and nervousness in combination with a diet designed to meet but not exceed caloric requirements. Authors’ address: Depts. of Clinical and Population Sciences and Veterinary Pathobiology, College of Veterinary Medicine, University of Minnesota, St. Paul, MN 55108. © 1999 AAEP.

1. Introduction

Chronic exertional rhabdomyolysis or “tying-up” is a common cause of disability in many breeds of horses. Some athletic horses have a sporadic episode of rhabdomyolysis that never recurs when treated with rest and a gradual return to work on a balanced diet with vitamin and mineral supplements. Sporadic cases of tying-up may be due to overexertion, exercise in excess of fitness state, dietary or electrolyte imbalances. Other horses, however, have repeated episodes of tying-up with very little exercise. In the past it has been assumed that all horses with chronic tying-up have the same underlying etiology. The focus of research in our laboratory has been to determine if there are multiple etiologies for tying-up, some of which may be breed-specific. The purpose of this study was to determine if chronic tying-up in Quarter Horses (QH) has the same underlying etiology as chronic tying-up in Thoroughbreds (TB).

2. Materials and Methods

A clinical protocol including history, physical exam, serum and urine chemistry, muscle biopsy, and exercise testing was applied to 21 TB and 30 QHs with chronic tying-up. Five of these Quarter Horses and five Thoroughbreds were purchased or donated to the University of Minnesota for further study. A muscle biopsy of the gluteus medius muscle from each horse was examined histochemically and biochemically. All donated horses performed an incremental standardized treadmill exercise test designed to achieve a heart rate of 200 bpm. Control horses of each breed were also evaluated. Muscle biopsies for glycogen and lactate determination were ob-
tained before and at the end of exercise. Subsequently, horses were exercised 4–5 days per week on a treadmill for three weeks to determine the pattern of change in serum CK with exercise. Pedigrees from each horse were obtained from the breed association dating back 5–7 generations. Intact muscle fibers were obtained from biopsies of the intercostal muscles for contractility testing. Muscle samples were placed in oxygenated physiological saline with the addition of various concentrations of caffeine. The concentration of caffeine required to induce a contracture (measured as normalized contracture force) was determined for each horse as well as for breed-matched controls. Intravenous glucose tolerance tests were performed on each horse using a standardized protocol as well as for breed matched controls.

3. Results

The muscle biopsies from the five Quarter Horses revealed muscle fiber necrosis and regeneration, subsarcolemmal vacuoles, a few fibers with centrally located nuclei, and a dark periodic acid–Schiff's (PAS) stain for glycogen. Abnormal PAS positive amylase-resistant inclusions were present in 2–30% of muscle fibers in Quarter Horses. Muscle biopsies from Thoroughbreds had numerous fibers with centrally located nuclei and normal PAS stains. Muscle glycogen concentrations in Quarter Horses were 1131 ± 96 mmol/kg dry weight compared with 501 ± 17 in Thoroughbreds.

The metabolic response to a standardized exercise test was similar among normal Thoroughbreds and the Thoroughbred with RER. Muscle glycogen concentrations declined by 17% in Thoroughbreds with and without a history of tying-up, and muscle lactates doubled following exercise. Muscle glycogen concentrations declined by 27% in Quarter Horses with tying-up and 24% in controls. Lactate concentrations increased by 4-fold in Quarter Horses that tied-up and 2.6-fold in controls. During daily treadmill exercise, CK was higher and remained elevated from the beginning of training in Quarter Horses, but was intermittently elevated in Thoroughbreds only after 2 weeks of training. The threshold for developing a muscle contracture in intercostal biopsies for Thoroughbreds with chronic tying-up was 5 mM of caffeine, significantly higher than the threshold of 1 mM for normal Thoroughbreds, the Quarter Horses with tying-up and normal Quarter Horses.

Quarter Horses given 0.5 mg/kg of glucose IV showed a similar peak in blood glucose concentration to the Thoroughbred horses with tying-up and normal Quarter Horses. A more rapid rate of decline in glucose concentrations at lower insulin levels, however, was seen in Quarter horses with abnormal polysaccharide in their muscles compared to Thoroughbreds with exertional rhabdomyolysis, or controls.

4. Discussion

Although the Quarter Horses and Thoroughbreds in this study had similar acute clinical signs of rhabdomyolysis, the underlying etiology appeared to be different for the 2 groups of horses. Quarter Horses were calm horses that had significant elevations in CK for the first 2–3 weeks of exercise. Thoroughbreds were more nervous horses that had intermittent elevations in CK after 2 weeks of training. The most notable difference between the 2 groups was the presence of PAS-positive inclusions in the muscle from the Thoroughbreds. This abnormal polysaccharide has previously been observed in a large number of Quarter Horses with chronic tying-up and has not been found in normal Quarter Horses. The term polysaccharide storage myopathy (PSSM) has been used to describe this muscle disorder, which is characterized by both increased muscle glycogen concentrations and abnormal muscle polysaccharide.

A number of myopathies have been described in humans which are associated with high muscle glycogen concentrations and increased CK with exercise. They are usually associated with an autosomal recessive deficiency in a glycolytic or glycogenolytic enzyme. The distinguishing metabolic response to exercise with such glycogen storage disorders is the inability of the muscle to metabolize glycogen during exercise and a failure of lactate concentrations to rise. The standardized exercise tests in the PSSM horses actually revealed a high anaerobic capacity in PSSM horses with marked lactate production during exercise. Since glycogen accumulation occurred in the face of normal glycogen metabolism, a glucose tolerance test was performed. The results of the glucose tolerance test suggest that glycogen storage in PSSM horses may be due to enhanced clearance of blood glucose from the bloodstream into the major insulin-sensitive tissue skeletal muscle. Further studies of glucose clearance and insulin sensitivity have been performed in PSSM horses which also confirm enhanced insulin sensitivity and glucose excursion from the blood stream with PSSM. Pedigree studies suggest that this is a heritable condition. Management of horses with PSSM includes regular daily exercise to enhance glucose and glycogen utilization as well as to enhance aerobic metabolism. Feeding a diet of grass hay and 1–4 lb of a rice bran supplement has also been found to be helpful for horses with PSSM by lowering blood glucose, insulin, and muscle glycogen concentrations.

The Thoroughbred horses with chronic tying-up did not have abnormal polysaccharide in their muscle fibers, had normal muscle glycogen concentrations, normal glucose tolerance tests, and normal metabolic responses to exercise. Thus, this condition in Thoroughbreds does not appear to be a metabolic myopathy. The Thoroughbreds with tying-up, unlike PSSM horses, had abnormal muscle contracture tests, similar to the myopathy called malignant hyperthermia (MH). MH is an inherited stress-
induced disorder that is commonly due to abnormal intracellular calcium regulation at the level of the calcium release channel (ryanodine receptor). Rhabdomyolysis in MH horses is intermittent and requires triggering factors such as halothane anesthesia, exercise, or excitement. Interestingly, Thoroughbreds with chronic tying-up also have a high incidence of myopathy following halothane anesthesia. Pedigree analysis of Thoroughbreds with chronic tying-up support a heritable basis for this condition. Thus we conclude that in some Thoroughbreds chronic tying-up is due to an abnormality in muscle contractility which may be induced by excitement, exercise, and halothane anesthesia. We have used the term recurrent exertional rhabdomyolysis (RER) for horses with this abnormality. Management of these horses seems best directed toward avoiding excitement and stress by changes in management, low soluble carbohydrate diets, tranquilization, and regular daily exercise. Dantrolene has been used in humans and swine to prevent MH, but its efficacy and dosage in horses has not been delineated.

In conclusion, tying-up is a syndrome that has several etiologies. A common cause of chronic tying-up in Quarter Horses is PSSM, which is best diagnosed by identifying abnormal polysaccharide in frozen muscle sections. In contrast, chronic tying-up in a proportion of Thoroughbreds appears associated with a heritable defect in muscle contraction. Specific diagnosis of this form of ER is done practically by history, physical examination, exercise testing, and the finding of numerous central nuclei in muscle biopsies. The caffeine contracture test is a very sensitive test for recurrent ER in Thoroughbreds, however, the requirements of an intact muscle and a specialized laboratory limit its practical application.

References