A nutritional review of polysaccharide storage myopathy

Polysaccharide storage myopathy is characterised as the dissolution of skeletal muscle in association with exercise. Genetic testing has uncovered two forms of polysaccharide storage myopathy: PSSM1 and PSSM2, and a subtype known as myofibrillar myopathy. Horses with these conditions can display a variety of symptoms. Nutritional management of PSSM1 and PSSM2 cases hinges on ensuring that rations are low in both starch and sugar, and daily exercise is also important for these horses.

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Fiona Watkins, Independent Equine Nutritionist, BSc, Pro Dip. Chennels West, Brook Lane, Albury Heath, Guildford, Surrey. GU5 9DH. Email: Fiona@thehorsenutritionist.co.uk

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Polysaccharide storage myopathy (PSSM) is also referred to as 'tying up', azoturia, Monday morning disease or exertional rhabdomyolysis syndrome (Frape, 2004). In simple terms, it is characterised as the dissolution of skeletal muscle in association with exercise. The term 'polysaccharide' refers to complex sugars stored in skeletal muscle.

Genetic testing now distinguishes two forms of PSSM and, more recently, a sub-type:

- Type 1 PSSM (PSSM1)
- Type 2 PSSM (PSSM2)
- Myofibrillar myopathy.

PSSM1 is caused by a genetic mutation in the glycogen synthase gene – glycogen is the storage form of starch and sugar. PSSM2 represents one, or more, other form of muscle disease that is characterised by abnormal staining of muscle glycogen in microscopic examination of muscle biopsies, while myofibrillar myopathy is described as an abnormal build-up of 'desmin' (a protein) in muscle tissue and myofibrillar degeneration (Valberg et al, 2017).

Type 1 PSSM

Type 1 PSSM was first described in detail by Valberg et al (1992) and is associated with a dominant mutation in the skeletal muscle glycogen synthase gene (GYS1). This gene mutation causes excessive storage of sugar (glycogen) in skeletal muscle (Valberg, 2017).

Suspected to be the result of an ancestral founder, the mutation is found in many different horse breeds worldwide, with some breeds, for example Percheron and Belgian Draft horses, having a particularly high disease prevalence (McCue et al, 2008). However, since it is very common that not all genetic mutations express themselves fully, PSSM1 can be asymptomatic in horses (Schwarz et al, 2011).

What are the clinical signs of PSSM1 in horses?

PSSM1 in horses is associated with a variety of clinical signs, including intermittent exertional rhabdomyolysis, muscle fasciculations, muscle atrophy, gait abnormalities and paresis (McCue et al, 2009). These symptoms are noted in conjunction with increased serum creatine kinase (CK) and aspartate transaminase (AST) activities (Valberg, 2018).

During these episodes, horses seem fatigued, lethargic, can have shifting lameness, tense their abdomen and can develop tremors on the flank region. When the horse stops moving, they may stretch out (as if about to urinate). They are often in pain, stiff, sweating and their muscles are firm to the touch, particularly on the hindquarters. Horses with PSSM1 can have a history of numerous episodes, although mildly affected horses may have only one or two episodes a year (Valberg, 2017).

Type 2 PSSM

PSSM2 equines are classified as those that have abnormal amylase-resistant polysaccharide (sugar) in their muscle biopsies, but do not have the glycogen synthase 1 mutation (Valberg et al, 2023). However, it should be noted that some muscle biopsies of this type are open to subjective interpretation. False positives can occur as there may not be a severe change in the muscle; therefore, the output may not be a clear positive or negative. Muscle biopsies are therefore

only recommended when horses are exhibiting clear symptoms of PSSM (Valberg et al, 2023).

What are the clinical signs of PSSM2 in horses?

In Arabians and Quarter Horses with PSSM2, the most common sign is tying up once again, with increased serum creatine kinase and aspartate transaminase (AST) activities.

Muscle atrophy and high serum creatine kinase activity is also reported as a common complaint in Quarter Horses with PSSM2.

In Warmblood horses, tying up may be reported, occasionally with high serum creatine kinase. However, the most common clinical signs of PSSM2 in Warmbloods are often most closely related to poor performance without elevations in serum creatine kinase activity. An undiagnosed gait abnormality, sore muscles and drop in energy level and unwillingness to perform after 5–10 minutes of exercise are common complaints with PSSM2. Warmbloods with PSSM2 can have painful, firm back and hindquarter muscles, reluctance to collect and engage the hindquarters, poor rounding over fences, gait abnormalities and slow onset of atrophy especially when out of work (Valberg, 2017).

Nutritional management and exercise for horses with PSSM1 and PSSM2

The mutation causing PSSM1 is a point mutation in the gene that codes for the skeletal muscle form of the glycogen synthase enzyme. As such, this mutation causes the glycogen synthase enzyme to be overactive, resulting in the constant over-supply and production of glycogen (Valberg, 2017). Correct nutritional management of PSSM1 cases, therefore, hinges on ensuring that rations are low in both starch and sugar (with high-fat levels, if additional energy is required as exercise levels increase) (Valberg et al, 1999).

The same nutritional and exercise regime prescribed for PSSM1 is also recommended for PSSM2 (Williams et al, 2018). The main guidelines being a reduction in feeds that promote muscle glycogen synthesis (i.e. starches and sugars), providing fat as an alternative fuel and promoting oxidative metabolism through exercise (Williams et al, 2018). Specifically, a ration should aim to provide:

- <20% of digestible energy as non-structural carbohydrate
- 15–25% of digestible energy as fat
- And daily exercise should be given.

<20% of digestible energy as non-structural carbohydrate

For both conditions, fibre/forage should form the basis of the ration; all horses should be receiving fibre (for example hay, grass or haylage) at a minimum of 1.5% of their own bodyweight (Harris et al, 2017) and the author recommends that this fibre should contain <12% non-structural carbohydrates for horses with PSSM1 (on a dry matter basis) in order to minimise post-feeding glycaemic responses (Harris et al, 2013). Therefore, soaking hay is recommended in order to achieve these levels (if hay analysis show non-structural carbohydrate levels higher than 12%). Horses with PSSM2, however, can tolerate slightly higher levels of non-structural carbohydrates; therefore, soaking hay is not necessarily recommended.

Valentine et al (2001) reported that effective dietary management required the elimination of grains, so all cereal-based feeds (such as wheat, barley and oats) as well as molasses, should be avoided. The author recommends that certain concentrate mixes and pellets that contain high levels of non-structural carbohydrates should be removed from the ration.

15-25% of digestible energy as fat

If the horse is lower in weight, or additional digestible energy is required as exercise levels increase, fat-based feeds, such as rice bran or linseed meal, can be introduced into the ration. (Valentine et al, 2001). The author also recommends that additional digestible energy can be delivered to the ration through the inclusion of oils, such as linseed oil.

As additional fat is recommended in the ration, vitamin E should also be supplemented. The reason for this is two-fold; firstly, increasing fat/oil in the ration increases the horse's requirement of vitamin E (Frape, 2004). Secondly, another possible mechanism of disease in glycogen storage diseases is free radical damage (Naylor et al, 2012). Vitamin E is the principal defence for reactive oxygen species in tissues, and skeletal muscle contains lower concentrations of vitamin E than other body organs (Jensen et al, 1990) and as such, may be more vulnerable to free radical damage, particularly in response to the large increases in metabolic demand that occur during exercise (Powers and Jackson, 2008).

Daily exercise

Diet alone will not improve the muscle function of horses with PSSM1 and PSSM2. Exercise is crucial in increasing mitochondrial capacity to oxidise fats (Williams et al, 2018).

It is recommended that horses should be warmed up with a long and low frame (Williams et al, 2018). Ideally, this should be done two or three times per week, particularly if the horse is sore across the back. Daily exercise is recommended, if possible – from as little as 10 minutes per day (Valberg, 2017) and when ridden, the horse should be given frequent breaks and the ability to stretch, in order to promote muscle relaxation (Williams et al, 2018).

For those horses displaying muscle atrophy, the addition of amino acid supplements or additional protein supplementation is recommended in order to increase muscle mass (Graham-Thiers and Kronfield, 2005).

Finally, often PSSM1 and PSSM2 equines are described as being 'in good body condition'; based on Carroll and Huntingdon's (1988) body condition scoring. Being in a 'good' condition would imply that the horse is carrying excess weight. Owners and veterinarians therefore need to ensure that the calorific intake of these horses is limited.

Myofibrillar myopathy

Myofibrillar myopathy is a newly identified muscular disorder that causes exercise intolerance in horses. It is a genetic condition, whereby muscle tissue is characterised by ectopic accumulation of desmin (a protein which is used in muscle contraction) and Z-disc and myofibrillar degeneration (Valberg et al, 2017). Myofibrillar myopathy is termed as such because, at a cellular level, the myofilaments that make up contractile proteins are seen to display an instability or disrupted alignment (Valberg, 2021).

What are the signs of myofibrillar myopathy in horses?

Myofibrillar myopathy has many of the same symptoms of PSSM2, in that horses look uncomfortable. They have an abnormal gait, vague lameness, alterations in the way of moving, do not appear to use their back properly, appear to have a lack of stamina, an unwillingness to go forward, inability to collect, abnormal canter transitions and an inability to sustain a normal canter (Valberg, 2021).

Dietary management of myofibrillar myopathy

As with PSSM1 and PSSM2, a nutritionally balanced diet with appropriate calorific intake and adequate protein, vitamins and minerals is essential. Forage should once again form the basis of the ration, with concentrates limited to no more than 20% as non-structural carbohydrates and fat used to deliver additional digestible energy requirements.

Amino acids

Additionally, whey-based proteins or supplements containing high levels of cysteine are recommended for horses with myofibrillar myopathy, as myofibrillar myopathy equines may have an increased cysteine requirement, based on alterations in genes involved in conversion of methionine to cysteine (found in Arabian horses with myofibrillar myopathy following exercise) (Valberg, 2021).

Due to the breaks in the myofilaments, the author additionally recommends specifically providing an amino acid supplement 45 minutes before or after the time of exercise, in order to provide the building blocks needed for the equine to build up their muscle mass (Valberg, 2021).

Antioxidants

Coenzyme Q10 is a key component of the first step in the mitochondrial electron transport chain. Warmblood horses with myofibrillar myopathy have been observed to have a decreased expression of proteins involved in the first step for this electron transport (Williams et al, 2021). When fed to healthy horses, cysteine and coenzyme Q10 were found to increase mitochondrial proteins (Valberg, 2021).

Exercise

Training programs for horses with myofibrillar myopathy vary depending on the severity of exercise intolerance. The horse may benefit from more rest between exercise bouts or lower-intensity exercise. Indeed, many owners of myofibrillar myopathy horses have found that 3 days of work followed by 2 days off work suits the horse best (Valberg, 2021). Initially, exercise should only be of a short duration (approximately 15–20 minutes in total). As the horse adjusts to treatment, the total ride time can be increased, gradually and slowly to approximately 30–45 minutes. Rest periods should be provided throughout the exercise to allow the horse to stretch their muscles.

Many horses benefit from a balance of work and rest to promote muscle recovery and tissue repair following exercise. A schedule of three work days followed by two rest days is believed to reduce stiffness and support post-exercise recovery (Valberg, 2021).

KEY POINTS

- Polysaccharide storage myopathy (PSSM) is characterised as the dissolution of skeletal muscle in association with exercise.
- Genetic testing now distinguishes two forms of PSSM – PSSM1 and PSSM2 – and more recently, a sub-type called myofibrillar myopathy, which causes exercise intolerance in horses
- PSSM1 in horses is associated with a variety of clinical signs, including intermittent exertional rhabdomyolysis, muscle fasciculations, muscle atrophy, gait abnormalities and paresis.
- Nutritional management of PSSM1 cases involves ensuring that rations are low in both starch and sugar (with high-fat levels, if additional energy is required as exercise levels increase).
- The same nutritional and exercise regime prescribed for PSSM1 is also recommended for PSSM2.
- Diet alone will not improve the muscle function of horses with PSSM1 and PSSM2. Exercise is crucial in increasing mitochondrial capacity to oxidise fats.

If possible, it is recommended that periods of complete inactivity are avoided and, instead, a consistent training routine is maintained for developing conditioning and preventing myofibrillar myopathy episodes.

Conclusions

The PSSM1 mutation causes the glycogen synthase enzyme to be overactive, resulting in the constant over-supply and production of glycogen. Both PSSM1 and PSSM2 have the same main nutritional guidelines including a reduction in feeds that promote muscle glycogen synthesis (i.e. starches and sugars), providing fat as an alternative fuel and promoting oxidative metabolism through exercise. For myofibrillar myopathy certain supplements may be recommended in addition to the general dietary changes. EQ

Conflicts of interest

The author declares that there are no conflicts of interest.

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