

Myofibrillar Myopathy

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Myofibrillar myopathy (MFM) is a recently identified disorder presenting with exercise intolerance or intermittent ER that is defined by specific histopathology.^{1,2} The hallmark histopathologic feature of MFM is cytoplasmic aggregates of the cytoskeletal protein desmin in scattered muscle fibers. Desmin functions to align sarcomeres at the Z-disc and tether them to the cell membrane. MFM may represent a more extreme subset of PSSM2 in Warmbloods and Arabians, but further research is required. The recommendations provided below are developed based on a muscle biopsy diagnosis of MFM and our research. They do not apply to horses diagnosed with MFM by genetic testing because we found no correlation between the results of the genetic tests for MFM and a muscle biopsy diagnosis of MFM.³

MFM in Warmbloods: Warmblood horses diagnosed with MFM by muscle biopsy have an insidious onset of exercise intolerance notable by 6-8 years of age characterized by a lack of stamina, unwillingness to go forward, inability to collect, abnormal canter transitions, and inability to sustain a normal canter.¹ Some PSSM2/MFM horses also have gastric ulcers⁴. Unresolved hindlimb lameness, stiffness, muscle pain and, rarely, an episode of ER are reported.⁵ Serum CK and AST activities are usually within normal limits unless samples are taken in conjunction with ER. A recent study found no association between commercial genetic tests for MFM and a clinical and histopathologic diagnosis of MFM in Warmblood horses.³

Arabians: Arabian endurance horses diagnosed with MFM usually have a history of intermittent elevations in serum CK activity after endurance rides (>10,000 U/L) or during exercise that follows a week or more of rest.² Horses do not always show the same degree of pain, sweating, and reluctance to move, as is frequently seen in other forms of acute ER. Myoglobinuria can be observed in horses with only mild muscle stiffness. Between episodes, the heart rate, lactate, CK, and AST responses to exercise are normal.

What causes MFM? The basis for MFM in Warmblood horses appears to be related to the individual effects of diet, exercise, and training on gene and protein responses to exercise with downstream effects on muscle mass, the alignment of contractile proteins, mitochondrial function, and oxidative stress (Williams et al in press). The basis for MFM in Arabian horses appears to be related to a need for enhanced cysteine synthesis, decreased cysteinebased antioxidants, and oxidative stress.⁶

Biochemical analysis of muscle biopsies in Arabians and Warmblood horses with PSSM2 has found that glycogen concentrations are similar to those of healthy breed-matched controls.^{5,7} Thus, the previous rationale for feeding a low NSC diet in these breeds does not appear to apply to WB or Arabian MFM horses. A subset of PSSM2 Arabian and Warmblood horses has been found to have a histologic marker called desmin aggregation that is the characteristic feature of MFM.¹ Based on these new findings and transcriptomic and proteomic analyses of muscle from horses with MFM, a new dietary approach has been developed.⁶

Management

Signs of muscle pain, atrophy and stiffness can be managed through specific diet and training regimes. Both diet and training must be changed to see a beneficial effect and a positive effect usually takes 4-6 weeks. At present, the best we can do is to use management techniques in order to reduce soreness and increase muscle mass. The recommendations provided are general recommendations.

Diet: Any changes in diet and exercise should be done in consultation with the veterinarian who provides primary care for your horse. Your veterinarian is aware of any musculoskeletal or metabolic issues pertinent to your horse that could be impacted by the recommendations below. Cases should receive a full physical examination by your veterinarian to ensure that there are no other underlying causes for performance problems.

Nutritionist: The detailed diet recommendations below are provided for your nutritionist to help balance your horse's diet. They can be presented by your veterinarian to the nutritionist at the company that provides your feed. We have also worked with an independent nutritionist, Katie Young, not associated with a particular feed company who can work with you for a fee to provide the recommended diet. Ktyoung60@gmail.com.

Because the caloric/nutrition needs and symptomology differ between MFM endurance Arabians capable of performing hours of aerobic exercise and MFM Warmbloods incapable of satisfactorily performing for 45 minutes, dietary approaches differ.

Nutrient Requirements: Rations should focus on providing quality protein and specific amino acids to aid in making the proteins necessary to rebuild the contractile proteins. Additionally, since oxidative stress is likely involved in the degenerative process, antioxidants or precursors of antioxidants are important to support the mitochondria.

Forage: MFM horses will typically consume 1.5-2% of body weight per day of hay. Good-quality grass or grass-legume mixed hays (55-65% NDF, 10-12% CP, 10-17% NSC) are preferable.

Energy Sources: There is no evidence that extremely low-NSC, high-fat diets are needed by Warmbloods with MFM and there does not appear to be a scientific reason why additional fat, a potential source of oxidative stress, would be of benefit to Warmbloods with MFM. Arabian endurance horses are typically fed higher fat diets, as Arabians depend more on fat oxidation than Thoroughbreds during exercise.⁸ However, since MFM in Arabian endurance horses is related to oxidative stress resulting from fat oxidation, it is questionable whether these horses need extremely high levels of fat intake (>15% total DE intake).

Concentrates: Both Warmbloods and Arabian endurance horses in the US are typically fed fairly low levels of concentrate with about 10% proteins. This may not have sufficient amino acids such as lysine, methionine, and threonine needed for muscle repair and generation of cysteine-based antioxidants. Leucine stimulates protein synthesis in the muscle post-exercise⁵⁰, which would be beneficial to MFM horses. Therefore, concentrates for MFM horses should include higher levels of protein (12-14% CP) containing high-quality amino acids and moderate levels of NSC (20-30%) and fat (4-8%). Potential commercial concentrates include a ration balancer that contains vitamins, minerals and at least 20%

protein may suffice for easy keepers. For horses that lack energy a diet such as sweet feed, Purina Omolene 400, Nutrena Triumph 12% or Purina Strategy are potential good concentrates for MFM when fed in the amount recommended on the bag by the manufacturer to get the proper balance of nutrients.

Supplements

Amino acids: For horses with symmetrical topline muscle atrophy and horses with MFM, amino acid supplements are currently recommended.^{1,9} Whey-based proteins are recommended because they are rich in cysteine. Cysteine is a key component of many antioxidants, and Arabian horses with MFM appear to have an increased cysteine requirement following exercise.⁶ We have recently worked with Kentucky Equine Research to develop an amino acid supplement for MFM that contains N-acetyl-cysteine and this is available with your veterinarians assistance from KER.com

Antioxidants: Horses with MFM have decreased expression of mitochondrial proteins and antioxidants in their muscle.⁶ Coenzyme Q10 (CoQ10) (Nano-Q10™, Kentucky Equine Research, KER.com) is a key component of the first step in the mitochondrial electron transport chain. Arabian and Warmblood horses with MFM have decreased expression of proteins involved in this first step. In healthy horses also fed amino acids, coenzyme Q10 increases mitochondrial proteins (Valberg unpublished). CoQ10 is used in human muscle disorders and is now being trialed as a supplement for MFM horses.

With any case of muscle atrophy, we like to ensure horses have normal serum vitamin E by measuring serum vit E and supplementing if necessary.

Exercise

Turn out: As much daily turn-out as possible in an area where the horse is encouraged to move about is recommended. Consult your veterinarian about grazing. Grazed-down grass-pastures appear to be fine for most MFM horses,

however, responses can be individual so consult with your veterinarian whether your individual horse can tolerate grazing.

Exercise: An equally important part of management is exercise. Consistent exercise increases turnover of structural proteins in the muscle to strengthen them and builds enzymes needed to burn energy as fuel. The number of days per week to ride varies with each horse. Many owners of MFM horses have found that three days of work then two days off works best for MFM horses. For some horses, exercise more frequently than three days in a row or rest more than two days in a row results in a stiff, difficult subsequent ride.

Beginning exercise: The decision to begin this work should be made in consultation with your veterinarian to ensure there are no underlying lameness issues that would be exacerbated by this exercise.

Warm-up: It works best for many horses to work in a round pen or on the longe-line after two weeks on the diet changes. Warm-up often works best if the horse is worked in a long and low frame for 10 -15 min. With this warm-up you are not looking for engagement of the hindquarters that can be built into the riding sessions; however, lifting of the back is desirable.

1) Aids that help create a long low frame on the longe line such as Vienna reins, double lunging, or a neck-stretcher are helpful. Side reins don't encourage enough stretch long and low.

2) Begin with a couple of minutes of walk with a low head carriage. Give a verbal good boy/girl each time the horse finds the correct stretched position so they know what you want.



3) Ask for a very relaxed trot to get the back swinging long and low without the need for hind limb impulsion to start. Watch to see the base of his neck muscles release, the back stretch and round up, and rump muscles contract and relax. To begin with, the length of time at a trot should be no more than 5 minutes in each direction. After that allow the horse to walk and stretch.

4) Ask for a few strides of canter, when the horse releases at the base of its neck at the canter I would do a few more strides then come back to trot and make sure the horse is moving well forward underneath him/herself. At the trot, try to get him/her to release the base of the neck and round the back while stretching down. Give a verbal good boy/girl each time the horse finds the correct position so they know what you want. Do several transitions for about 4 min then walk and stretch.

5) Work the horse in both directions. Ideally, keep the horse on a circle that is close to 20 m. By moving the circle up and down the ring as you are lunging if there is room, you can also allow your horse to have some breaks from constantly circling.

6) After a few weeks, add longer canter periods with push from behind and continue for as long as the horse can carry himself with a relaxed base of his neck, impulsion and rounded back. If this does not come within a minute go back to trot work and try this duration of canter again in a week. It takes several weeks in my experience to get them to round at a canter through their back. They often cannot hold the canter at first for more than a few strides in the correct position. Once this is working well add more transitions.

7) With time and clinical improvement, some horses can start under-saddle without being first lunged.

Horses that refuse to go forward: If horses are refusing to go forward for no foreseen reason after 3 weeks of the diet change, reinforcing the go command may be necessary. Consult your veterinarian prior to this exercise to ensure there are no health risks and consider help from a professional. This work is most easily done in a round pen or small arena following the above warm up exercise and with the assistance of a trainer. Ask the horse verbally to trot and move forward and if no response occurs re-enforce with a startling sound (snapped lunge whip, shaking plastic bags, tin cans with coins, loud noise). Work on this with a cue that says clearly when you say go it means go rapidly forward. Ensure you get a response. When you begin to ride, have your trainer, use the re-enforcement to link the verbal forward cue to the leg on, and if necessary, the scary noise to re-enforce the leg means go forward. Horses with MFM can develop behavioral problems because they associated exercise with pain. Caught early, we have found that the diet and exercise regime and training can help overcome this problem.

Strengthening exercises: Cavaletti, hill work, small jumps can all help to build strength. The exercises in Narelle Stubbs and Hilary Clayton's book "Activating your horse's core" are good as well (Amazon.com). Underwater treadmill exercise would also be of benefit to these horses. Theraband exercise (a stretchy wide rubber band that goes around the hind quarters and attaches to the saddle pad) can be considered after the initial low, low stretch warm-up work, and after the horse can trot forward easily, but should be gradually introduced (first while lunging and eventually under saddle). See <http://equicoreconcepts.com/system.html>

Riding: The long and low warm-up with adequate stretching is recommended before riding. This should be performed both at the trot and canter (once the horse is able). When riding you can begin to introduce period of work on the bit with hindend engagement. Rest periods that allow the horse to relax and stretch their muscles between 2 – 5 min periods of collection under saddle may be of benefit. The collected work should be performed in intervals lasting no more than 5 min with a period of stretching (either at trot or walk) provided between intervals. The time of active collection can be gradually increased as the horse works more underneath himself and in balance. Total ride times in horses with MFM appear to be most productive if kept between 30-45 minutes, with horses just starting out having rides between 15-20 minutes (including walking).

References

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