

Disclaimer: This document is not intended to provide definitive guidance on diagnosis and treatment of patients with Muscular Dystrophy. It provides clinicians with general information on certain disease processes that may assist in clinical decision making. Specifically, Empi/VitalStim is not aware of any published empirical data on the use of NMES for dysphagia in this patient population and has not requested nor received specific clearance from the US FDA for such labeling. Clinicians are advised to consult the professional literature for information specific to that condition and use best practice guidelines in determining treatment intervention.

Background

Muscular dystrophy (MD) refers to a group of over 30 genetic diseases which are characterized by progressive skeletal muscle weakness, deficits in muscle proteins, and death of muscle cells and tissue. Each form of muscular dystrophy is caused by a genetic mutation that is particular to that type of the disease.¹ Because the pathology of the disease varies, the different forms of MD differ in terms of the extent of weakness, the age of onset, and the rate of progression.²

Reports on the incidence of dysphagia with the different forms of MD vary significantly; not all types of MD result in dysphagia. Dysphagia is very prevalent in oculopharyngeal MD, but is not considered a “key” symptom with most forms of MD. Willig et al. reported significant swallowing problems in as high as 38% of patients with limb-girdle muscular dystrophy, 33% of those with myotonic muscular dystrophy, 20% with Duchenne muscular dystrophy, and 6% of those with facioscapulohumeral dystrophy.³

Pathophysiology and Presentation

Muscles are made up of bundles of fibers (cells). Groups of proteins along the membrane surrounding each fiber and within the cell help to keep muscle cells working properly. When one of these proteins is absent or inadequate (because of a genetic deficit), the result can be muscular dystrophy. Absence of or defects in different proteins are the main causes for muscular dystrophy.⁴

Oculopharyngeal MD (OMD) is characterized initially by drooping of the eyelids, followed by weakness of the muscles of the face and throat, resulting in difficulty swallowing. Signs and symptoms first appear in adulthood, usually in a person's 40s or 50s.¹ Progression is slow. It is believed that OMD is due to a defective gene which is suspected to lead to production of extra chemical material that causes formation of clumps in the muscle cells.⁴

Limb Girdle Muscular Dystrophy (LGMD) refers to a group of types of MD that primarily affect the voluntary muscles around the hips and shoulders. The proximal muscles are most affected with distal muscles affected in the later stages, if at all. The genes associated with LGMD normally make proteins necessary for muscle function. With this disease some of these proteins are missing, which is thought to cause the cell membrane to lose some of its “shock absorbing” qualities, thereby decreasing its ability to protect the muscle cell from injury during normal contraction and relaxation cycles. In LGMD, certain kinds of high intensity, stress-causing exercises may actually hasten muscle damage.⁴

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Myotonic MD (MMD), also known as Steinert's disease, is the most common adult form of the disease. There are two variations of this form of MD: MMD1 and MMD2. MMD1 is the more common form of this disease. The distal muscles are affected first in MMD1, as opposed to the proximal muscles in MMD2. Both types of this form of muscular dystrophy produce stiffness of muscles and an inability to relax the muscles at will (myotonia). Muscle weakness (both smooth and skeletal) is also a prominent feature.¹ MMD is characterized by cataracts, cardiac abnormalities, and endocrine disturbances.² Facial weakness and weakness of the respiratory muscles necessary for coughing are more common in MMD1.⁴

Duchenne's MD (DMD) is the most common pediatric form of MD. It primarily affects boys with an onset between 3-5 years of age with rapid progression. This form of MD is caused by an absence of dystrophin, which is a protein involved in maintaining structural muscle integrity.² Symptoms include frequent falls, weakness in lower leg muscles resulting in difficulty running or jumping, and in some cases mild mental retardation.¹

Facioscapulohumeral Dystrophy (FSHD) usually begins in the teenage years. It causes progressive weakness in muscles of the face, arms, legs, and around the shoulders and chest. It progresses slowly and can vary in symptoms from mild to disabling.² Dysphagia is not typically considered a significant symptom of this disease.

Typical dysphagia dysfunction by disease type

OPMD: pharyngeal constriction weakness, decreased UES opening, and esophageal issues. Most patients report difficulty initially with swallowing food, particularly dry food. As the disease progresses, liquids may become difficult to swallow as well. In a study of 14 patients with OPMD, 82% presented with tongue atrophy and weakness, 67% with dysphonia, and 43% with facial muscle weakness.⁷

LGMD: intact oropharyngeal transit but with a delay of hypopharyngeal transit. A CP bar is often present.

MMD: intact oropharyngeal transit but with a delay of hypopharyngeal transit. Vallecular and pyriform sinus pooling may be present as well as velopharyngeal incompetence, decreased esophageal contraction, and reduced UES pressure.⁶

DM: decreased bite force. Pharyngeal transit may be normal to mildly prolonged with mild vallecular and pyriform sinus pooling. Decreased esophageal motility may be present.⁶

FSHD: mild involvement of the jaw and lingual muscles. Dysphagia is seldom life threatening.⁵

Management

There is no specific treatment to stop or reverse any form of MD. Drug therapy includes corticosteroids to slow muscle degeneration, anticonvulsants to control seizures, immunosuppressants to delay some damage to dying muscle cells, and antibiotics to fight respiratory infections.²

Guidance from the literature: Muscular Dystrophy

Dysphagia management: Doctors and therapists have somewhat different opinions on the relative value or danger of various exercise regimens in people with muscular dystrophy (see “literature regarding exercise” below). In general, the research is inconclusive about the effectiveness of exercise, with or without NMES, for patients with MD. Because of this, dysphagia management currently often consists primarily of compensatory interventions and maneuvers to increase safety as opposed to active therapeutic exercise aimed at improving swallowing function.

Several studies have shown the effectiveness of a cricopharyngeal myotomy for patients with MD (see Coiffier et al. below), but in general the positive effects of the procedure are short lived for some patients, especially as the disease continues to progress.

Literature review

Hill M, Hughes T, Milford C. Treatment for swallowing difficulties (dysphagia) in chronic muscle disease. *Cochrane Database Syst Rev.* 2004; (2):CD004303.

OBJECTIVES: Our objective was to determine the most appropriate intervention for dysphagia in people with chronic, untreatable, non-inflammatory muscle disease. **SELECTION CRITERIA:** We included randomized and quasi-randomized controlled trials of adults and children with chronic untreatable non-inflammatory muscle disease. The interventions under review included dietary modification, swallowing maneuvers, a range of surgical interventions and enteral feeding. **MAIN RESULTS:** No studies were found that fulfilled the inclusion criteria. Therefore it was not possible to determine the benefit or otherwise of surgical intervention (cricopharyngeal myotomy or upper esophageal dilatation) for oculopharyngeal muscular dystrophy or other chronic progressive muscle diseases, and dietary advice or enteral feeding for children with congenital myopathy, compared with no intervention or an alternative intervention. **REVIEWERS' CONCLUSIONS:** **There are no trials that have adequately evaluated treatments in the management of dysphagia for chronic muscle disease.** It is therefore not possible to decide on the most appropriate treatment for a given individual based on current evidence.

Coiffier L, Périé S, Laforêt P, Eymard B, St Guily JL. Long-term results of cricopharyngeal myotomy in oculopharyngeal muscular dystrophy. *Otolaryngol Head Neck Surg.* 2006; Aug 135 (2):218-22.

OBJECTIVE: To analyze long-term results of extramucosal cricopharyngeal myotomy in oculopharyngeal muscular dystrophy. **RESULTS:** In the short term, 25 patients showed a complete remission of symptoms, 10 showed a marked improvement, and 4 exhibited no improvement at all (success rate of 90%). Long-term evaluation during a mean follow-up of 4 years showed that of the 35 improved patients, 12 exhibited a recurrence of dysphagia (mean time of 39 months). **CONCLUSION:** **Extramucosal cricopharyngeal myotomy improves dysphagia in oculopharyngeal muscular dystrophy patients during the first few years but one third of the patients exhibited a recurrence of symptoms within 3 years.**

Literature regarding exercise and NMES with MD

The research is varied with regards to the effectiveness of exercise for patients with MD. This is in large part due to the biological variations between the various disease types. Studies claiming either positive or negative treatment effects of exercise in one type of MD have thus got limited relevance to other types of MD. The literature is generally inconclusive about the therapeutic benefit of exercise in patients who have MD. There is minimal, if any, published research on the use of NMES with this population.

Ansved T. Muscle training in muscular dystrophies. *Acta Physiol Scand.* 2001 Mar; 171 (3):359-66.

There has been a debate for many years on whether muscular training is beneficial or harmful for patients with myopathic disorders and the role of exercise training in the management of these patients is still controversial. Much of this confusion is because of the lack of well-designed controlled training studies on this heterogenic group of disorders. Because effective therapies are still lacking, the patients have to rely on symptomatic treatment in which continuous physiotherapy plays an important role. There is thus still a need for studies evaluating the short- and long-term effects of muscular training in different types of myopathic disorders. We need to elucidate whether muscular training can increase strength and resistance to fatigue, but most importantly, we need to clarify whether training can improve specific functional abilities of the patient with myopathy. Future studies should give us specific information on what type of training, endurance or strength training, is to be preferred for different myopathies. The effect of strength training in one type of muscle disorder is not directly applicable to another, but is largely dependent on the underlying biological defect. From the studies published so far, high-resistance strength training at submaximal and possibly also at near-maximal levels seem beneficial, at least in the short perspective for slowly progressive myopathic disorders. However, the long-term effects of such training have not been systematically studied. In rapidly progressive myopathies, which are caused by deficient structural proteins such as in Duchenne's muscular dystrophy, the use of high-resistance training is far more controversial and questionable. **If exercise regimens are to be used, they should preferably commence in the early stages of the disease, at which time there is still a substantial amount of trainable muscle fibers.**

Tollbäck A, Eriksson S, Wredenberg A, Jenner G, Vargas R, Borg K, Ansved T. Effects of high resistance training in patients with myotonic dystrophy. *Scand J Rehabil Med.* 1999; 31 (1):9-16.

Nine ambulatory subjects with myotonic dystrophy participated in a supervised 12-week progressive high-resistance training program. Knee extensor muscles were trained 3 times a week with free weights. One leg was randomly chosen for training and the other served as control. Six patients completed the training program. There

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was no difference between pre- and post-training concentric or eccentric isokinetic values at 30 degrees/second in either leg. Muscle biopsy in the trained leg revealed no difference in the degree of histopathological abnormalities before and after training. After training, there was a tendency toward increase in cross-sectional area of type I muscle fibers. However, the number of subjects was too small to draw conclusions regarding the effects of training on the histopathological changes. **In conclusion, patients with myotonic dystrophy improved their muscle strength without any observed negative side effects after a 12-week high-resistance training program.**

van der Kooi EL, Kalkman JS, Lindeman E, Hendriks JC, van Engelen BG, Bleijenberg G, Padberg GW. Effects of training and albuterol on pain and fatigue in facioscapulohumeral muscular dystrophy. *J Neurol* 2007. Jul; 254 (7): 931-40.

METHODS : Sixty-five patients were randomized to strength training of elbow flexors and ankle dorsiflexors or non-training. After 26 weeks, albuterol was added in a randomized, double-blind, placebo-controlled design. **RESULTS :** Eighty percent of patients reported chronic persistent or periodic, multifocal pains. Thirty-four percent of the participants were severely fatigued. Strength training and albuterol failed to have a significant effect on all outcomes. **CONCLUSIONS :** Pain and fatigue are important features in FSHD. **Strength training and albuterol do not have a positive or negative effect on pain, experienced fatigue, functional status and psychological distress.**

Grange RW, Call JA. Recommendations to define exercise prescription for Duchenne muscular dystrophy. *Exerc Sport Sci Rev.* 2007 Jan; 35(1): 12-7.

Duchenne muscular dystrophy yields pervasive and progressive muscle weakness. This weakness may be attenuated by regular, low-intensity exercise. **However, there is a critical lack of data to support appropriate exercise prescription.** Because inappropriate activity may exacerbate the dystrophic process, a systematic analysis of muscle function to determine potential exercise load thresholds to avoid injury in dystrophic mice and dogs, and then in humans, is recommended.

Sveen ML, Jeppesen TD, Hauerslev S, Krag TO, Vissing J. Endurance training: an effective and safe treatment for patients with LGMD21. *Neurology*, 2007; Jan 2; 68(1) 59-61.

We studied the effect of aerobic training on conditioning in patients with limb-girdle muscular dystrophy type 2I (LGMD2I). Nine patients with LGMD2I cycled fifty 30-minute sessions at 65% of their maximal oxygen uptake over 12 weeks. Training significantly improved work capacity, paralleled by self-reported improvements. Creatine kinase levels did not increase significantly, and muscle morphology was unaffected. **Moderate-intensity endurance training is a safe method to increase exercise performance and daily function in patients with LGMD2I.**

Ansved T. Muscular dystrophies: influence of physical conditioning on the disease evolution. *Curr Opin Clin Nutr Metab Care.* 2003 Jul; 6(4):435-9.

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RECENT FINDINGS: Although the usefulness of exercise training in muscular dystrophy patients has been debated for many years, only a limited number of articles addressing this issue have been published to date. Existing studies on the effects of strength training in patients with muscular dystrophies have shown promising results, but interpretations are hampered by several methodological shortcomings.

SUMMARY: The scientific basis for solid recommendations of different exercise regimens in muscular dystrophies is poor, but existing data suggest beneficial effects of adopting an active lifestyle. **Low- to moderate-intensity resistance and aerobic training may be recommended in slowly progressive myopathic disorders.** To date, there is no evidence to support the recommendation of high-resistance exercise regimens over low-moderate intensity exercise. In rapidly progressive myopathies, which are due to aberrant structural proteins such as Duchenne muscular dystrophy, the use of high-resistance and eccentric training should be avoided. **There is still, however, no evidence that physical training can influence the evolution of muscular dystrophies in the long term.**

Carter GT, Abresch RT, Fowler WM Jr. Adaptations to exercise training and contraction-induced muscle injury in animal models of muscular dystrophy. *Am J Phys Med Rehabil.* 2002 Nov; 81(11Suppl):s151-61.

This article reviews the current status of exercise training and contraction-induced muscle-injury investigations in animal models of muscular dystrophy. Most exercise-training studies have compared the adaptations of normal and dystrophic muscles with exercise. There is some evidence in animal models that diseased muscle can adapt and respond to mechanical stress. However, exercise-injury studies show that dystrophic muscles have an increased susceptibility to high mechanical forces. Most of the studies involving exercise training have shown that muscle adaptations in dystrophic animals were qualitatively similar to the adaptations observed in control muscle. **Deleterious effects of the dystrophy usually occur only in older animals with advanced muscle fiber degeneration or after high-resistive eccentric training.** The main limitations in applying these conclusions to humans are the differences in phenotypic expression between humans and genetically homologous animal models and in the significant biomechanical differences between humans and these animal models.

Given the wide range of findings about exercise with patients who have MD, it is difficult to make definitive conclusions about what should be done in therapy. However in general, patients in the early stages of MD are more likely to possibly benefit from exercise treatment than those in the later stages who may not have sufficiently intact muscle fibers remaining to make improvements in strength. As with other progressive conditions, low to moderate intensity exercise is preferred over high intensity activities which should be avoided. With patients who present with more severe forms of MD for whom exercise may no longer be indicated, speech pathology may be provided as more of a consultative role in offering safe diet recommendations and swallowing strategies to manage rather than treat the dysphagia.

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