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Physical exercise in adults with hereditary neuromuscular disease

CLINICAL REVIEW

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Hereditary neuromuscular diseases are a heterogeneous group of disorders that may manifest at birth, although symptoms may also emerge in childhood or adulthood. Persons with hereditary neuromuscular diseases have previously been advised to avoid strenuous physical activity for fear that exercise would damage their already weakened muscles. Recent studies show that physical activity and exercise can be beneficial, but must be tailored to individuals on the basis of their diagnosis and functional level.

This article concerns hereditary myopathies and muscular dystrophies in adults (Table 1), and is based on a discretionary selection of reviews and original articles, as well as the authors' clinical experience with this patient population.

All of these neuromuscular diseases predominantly affect skeletal muscle; however, they may affect other organs too, especially the heart (1). The pattern of inheritance may be dominant, recessive or sex-linked (1). Most of the disorders are progressive; some progress quickly whereas others remain relatively stable over time (2). The disease course varies depending on the specific neuromuscular disorder, but major individual differences may be seen even among patients with the same genetic mutation. Much progress has been made in the diagnosis of neuromuscular diseases, and umbrella terms such as limb-girdle muscular dystrophy now include numerous genetically defined subgroups (1). A specific genetic diagnosis can provide insights into the particular challenges associated with a given disease variant. This knowledge is important for being able to offer appropriate guidance and advice on exercise and physical activity.

Table 1

Examples of hereditary neuromuscular diseases. AD = autosomal dominant, AR = autosomal recessive

Disorder type	Disorder	Inheritance
Muscular dystrophies	Duchenne/Becker	X-linked
	Emery-Dreifuss	X-linked AD/AR
	Facioscapulohumeral	AD
	Limb-girdle	AD/AR
Disorders of cell membrane excitability, and myotonias	Myotonic dystrophies type I and II	AD
	Congenital myotonia	AD/AR
	Periodic paralysis	AD
Congenital muscular dystrophies/myopathies	Central core	AD
	Nemaline	AD/AR
	Ullrich/Bethlem	AD/AR
Distal myopathies	Welander	AD
	Distal titinopathy	AD/AR
Metabolic myopathies	McArdle	AR
	Mitochondrial myopathies	Mitochondrial inheritance/X-linked/AD/AR

We know from the normal population that lack of exercise and a sedentary lifestyle can lead to health problems and disease (3). Moreover, physical activity can, to some extent, prevent chronic disease and have a positive effect on conditions such as depression and pain (4). Recommendations have been developed for physical activity both for the general population and for persons

in poor health (5). However, this is general advice that does not necessarily apply specifically to individuals with neuromuscular disease (4). We know that lack of physical activity may lead to further loss of muscle mass, reduced walking distance and increased risk of overweight, fatigue and pain in persons with neuromuscular disease (4). An increase in activity levels must be tailored to each individual in accordance with his/her interests, wishes and functional level, and should contribute to a feeling of coping. Physical activity need not be synonymous with organised exercise, but may include everyday activities in which fitness, strength and mobility are challenged with appropriate frequency, duration and intensity (5).

Complications relevant to exercise

Weakness, stiffness and contractures

Neuromuscular disorders are primarily associated with muscle weakness, the distribution of which differs between subgroups (1, 2). A distinction is often made between proximal and distal muscle weakness. In some disorders, there may also be significant weakening of back and abdominal muscles (6). Muscle stiffness (myotonia) is typically seen, especially in myotonic dystrophy, but also in other neuromuscular diseases (2). Contractures are common (7) and occur as a result of an imbalance in the muscles around a joint and a reduced ability to use the muscles. They may also be a consequence of the dystrophic process, as in Emery-Dreifuss muscular dystrophy and Ullrich congenital muscular dystrophy (1). Contractures may result in secondary impairments and difficulties in using otherwise functional muscles.

Pain and fatigue

Pain has been seldom studied in patients with hereditary neuromuscular diseases (7), but is often reported by the patients themselves. Pain may be a consequence of secondary changes such as stiffness or suboptimal movements of the body, but it may also be a hallmark of the disease itself, as in facioscapulohumeral muscular dystrophy (8). Fatigue is another common challenge for patients with neuromuscular disease (7, 9). Exercise of an appropriate type and amount may be beneficial in combatting fatigue (8, 10, 11).

Elevated creatine kinase levels

Some muscular dystrophies and metabolic myopathies are associated with an increased risk of rhabdomyolysis (2). Rhabdomyolysis is characterised by an acute increase in levels of the muscle enzyme creatine kinase (CK) owing to extensive damage to muscle cells (12). Myoglobin deposition in the kidneys as a consequence of such acute damage may be treated, if necessary, with forced alkaline diuresis (12). In healthy individuals, a CK level > 5 000 IU/l is proposed to indicate treatment-requiring rhabdomyolysis (12). Elevated CK levels are common in neuromuscular disease, although levels may be normal in

slowly progressive myopathy and certain muscular dystrophies (2). It is important to be aware that some patients with muscular dystrophies may have significantly increased CK levels without displaying symptoms of rhabdomyolysis. Sensible exercise programmes will not normally lead to dangerous increases in CK levels in patients with neuromuscular diseases. Nevertheless, it is useful to know which variant of hereditary muscle disease a patient has, in order to assess the risk of triggering rhabdomyolysis.

Cardiac involvement

Cardiac involvement is common in some neuromuscular diseases (13). These include many muscular dystrophies (Duchenne, Becker and Emery-Dreifuss muscular dystrophies, myotonic dystrophy types 1 and 2, limb-girdle muscular dystrophy types 1B, 2C–F, 2G and 2I) (13) and certain congenital myopathies (14). Cardiac involvement may manifest as cardiomyopathy or cardiac arrhythmias (14). For some neuromuscular diseases such as limb-girdle muscular dystrophy type 1B (laminopathy), cardiac involvement may be the first and sometimes the only sign of neuromuscular disease (13). The most common variant of limb-girdle muscular dystrophy in Norway, type 2I, may give rise to dilated cardiomyopathy and conduction disease (13). In cases of known or suspected cardiac involvement, therefore, it is important for the patient to be monitored by a cardiologist irrespective of whether or not they have symptoms (13, 14). In neuromuscular diseases known to affect cardiac muscle, it is usually safe to exercise, but advice on physical activity must be given after consultation with a cardiologist and preferably following a cardiac examination (13).

Respiratory muscle involvement

Some neuromuscular diseases affect respiration, mainly as a result of weakening of the respiratory muscles (15). This is the case in some metabolic myopathies and mitochondrial myopathies, as well as in congenital myopathies and a number of muscular dystrophies (Duchenne, Becker, Emery-Dreifuss and facioscapulohumeral muscular dystrophy, myotonic dystrophy type 1, and limb-girdle muscular dystrophy types 2A and 2I) (2). Endurance training, strength training and training of respiratory muscles can be helpful, and studies have shown improvements in daily activities, quality of life and oxygen uptake (VO_2 max) (15). It has been shown that aerobic exercise and strength training are likely to be effective in patients with neuromuscular disease, and that cardiovascular changes due to exercise are comparable with those seen in healthy persons (15). Respiratory training in neuromuscular diseases is somewhat controversial and requires specific knowledge of pulmonary physiotherapy and of the particular neuromuscular disorder in question (15). In cases of severe restrictive pulmonary impairment, it is not certain that respiratory training is beneficial, and it is important to be familiar with various breathing aids (15).

Recommended physiotherapy and exercise

Physiotherapy

Persons with a hereditary neuromuscular disease should be referred for physiotherapy. The muscle weakness, stiffness and pain associated with a neuromuscular disease may result in suboptimal compensatory body movements. Physiotherapists have specialist expertise in evaluating the musculoskeletal system and can assess the challenges facing individual patients, as well as their capabilities (7). They can perform a personalised assessment of movement strategies and patterns and put in place measures to help the individual to use his/her body more effectively in everyday life and during exercise. This evaluation is also integral to making recommendations regarding exercises, aids, activity adjustment and everyday training load.

Problems with balance are common in persons with neuromuscular disease (7). Balance training can improve bodily awareness and confidence in maintaining balance, and reduce the risk of falls (7). Walking aids and other activity aids must be evaluated continuously (8). This often means balancing the wish to maintain activity levels and independent mobility against the risk of falls and injuries. Preventative measures in the form of exercise to maintain range of movement and muscle length, with the use of orthoses if appropriate, are also important. It may be necessary to evaluate the current use of aids, as well as sitting and lying positions. Immobilisation after severe fractures often leads to accelerated loss of function in those with neuromuscular diseases.

Exercise

Persons with neuromuscular disease were previously advised to avoid exercise because it was thought to be harmful for weakened muscles (3), and because it was unclear whether exercise would have any effect. More recently, studies have shown that tailored physical activity, such as aerobic training on a bicycle or moderate strength training, can be beneficial for persons with neuromuscular disease (3, 4, 10). CK measurements and studies of muscle biopsies have not revealed signs of exercise-induced muscle injury in these patients (8, 11). Therefore, the recommendation is no longer for patients to avoid training, but instead for training to be tailored to each patient in accordance with their diagnosis and functional level (3, 4, 7, 10).

Strength training

The studies that have been conducted on strength training have been small, usually with mixed intervention groups and often without control groups (10, 16). The results of these studies must therefore be interpreted with caution. The aim of training is to maintain existing strength or reduce the progression of muscle weakness, and not necessarily to strengthen the affected muscles (7). Any increase in muscle strength is probably the result of effects on muscles that are relatively unaffected by the neuromuscular disease, but which may be

deconditioned as a result of inactivity (10). Low intensity strength training (10–15 repetitions) may be beneficial for persons with sufficient muscle strength to move against gravity (4). There is no evidence that heavy strength training has additional beneficial effects beyond those of moderate exercise, and such training should therefore be avoided as it may lead to overloading of muscles (4). Heavy eccentric strength training is not recommended either for the same reason (9). The latter is also thought to be a frequent cause of serious muscle injury in those without neuromuscular disease (12). Studies of limb-girdle muscular dystrophy, facioscapulohumeral muscular dystrophy, myotonic dystrophy type 1 and mitochondrial myopathies have shown that moderate strength training is safe and can have an impact on muscle strength and endurance, but results vary (3, 4, 9). Although studies generally point towards beneficial effects of moderate strength training, there is not yet sufficient evidence to make general recommendations for patients with neuromuscular diseases (10, 16). Major individual differences are seen in the intensity of training that can be tolerated, both between patients with different muscle diseases and among those with the same genetic disease variant.

Endurance training

Moderate endurance training in which the muscles receive an adequate supply of oxygen, but the individual may become slightly out of breath, can improve cardiovascular function in persons with neuromuscular disease (4). In small studies of limb-girdle muscular dystrophy (9), myotonic dystrophy type 1, metabolic myopathy (McArdle's disease) and mitochondrial myopathies, endurance training was not harmful and had a moderately beneficial effect (3, 4). Studies of ergometer cycling in patients with facioscapulohumeral muscular dystrophy have also shown that this is safe and may improve endurance (8, 11). Bodyweight-supported treadmill training and pool training are other examples of exercise that some may enjoy and that may potentially improve endurance (3).

Summary

Our recommendation is to avoid the inactivity that would otherwise lead to increased deconditioning and further reduction in muscle strength beyond that caused by the primary neuromuscular disease. Such deconditioning and loss of strength may in turn increase fatigue and pain, and decrease mobility and functioning. Appropriate training and physical activity is generally safe, but must be tailored to the individual on the basis of his/her diagnosis, functional level and lifestyle.

Tailored physical activity that takes into account disease-specific issues is recommended as it may facilitate daily activities and improve physical fitness. For advice on appropriate forms of activity, it may be useful to consult a physiotherapist with knowledge of neurology and experience in creating personalised exercise plans with appropriate amounts and types of training.

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