Review

Nutrition for boys with Duchenne muscular dystrophy

Sarah Leighton

Abstract

Duchenne muscular dystrophy is one of the most common genetic disorders. Considerable research has been dedicated to preventing or treating this condition, yet little information is available with regard to nutrition. This review of recent literature gives an overview of Duchenne muscular dystrophy and presents recent research relating to nutrition for boys with this condition. Education of families and good nutrition from an early age contributes substantially towards individual quality of life. The energy and protein requirements of boys with Duchenne muscular dystrophy are quite specific. It may be that supplements of amino acids, such as glutamine, arginine and vitamin E and of micronutrients, such as vitamin E, biotin, coenzyme Q10, as well as n-3 fatty acids will prove useful. Further research is indicated. Although nutrition will not alter the ultimate outcome, it is an important component in the optimum care of boys with Duchenne muscular dystrophy.

Key words: Duchenne muscular dystrophy, muscular dystrophy, nutrition, diet

About Duchenne muscular dystrophy

Duchenne muscular dystrophy (DMD) is the most common of the muscular dystrophies. It is a progressive, degenerative myopathy. It is an inherited X-linked recessive condition, affecting approximately 1:3300 male births. The primary abnormality is an absence of dystrophin, a protein normally found at the cytoplasmic face of the muscle cell surface membrane. Dystrophin provides mechanical reinforcement to muscle fibres, apparently helping to protect them from the potentially damaging tissue stresses developed during muscle contraction (1). It has been postulated that the lack of this and other associated transmembrane glycoproteins results in an unstable muscle cell membrane and impaired intracellular homeostasis (2).

Serum creatine kinase activity is increased in patients suffering from various muscular dystrophies. It is proposed that the absence of dystrophin in DMD muscle may result in temporal damage to the lipid membrane bilayer during muscle contraction allowing the passage of creatine kinase (3).

Duchenne muscular dystrophy is associated with a marked loss of muscle mass (4). Skeletal muscles are affected (initially the quadriceps and gluteal muscles) as are the respiratory muscles and cardiac myocytes. As the membranes of muscle fibres degrade, the fibres are replaced initially by a proliferation of connective tissue, and later by fat. Eventually there are only residual islets of muscle fibres in a sea of fat.

Boys with DMD need to maintain walking for as long as possible. Even short periods of immobility (associated with minor illness or trauma) can lead to marked loss of muscle power. As the condition progresses, boys are usually wheelchair bound from seven to nine years of age. Respiratory problems occur due to a restrictive deficit from weak intercostal and associated muscles. Vital capacity plateaus in boys with DMD in their early teens and then steadily declines, predisposing to nocturnal hypoventilation and hypoxia, which may improve with assisted night-time ventilation. A marked scoliosis usually develops during the adolescent growth phase, when weakened muscles cannot keep up with the rate of bone growth. Spinal fusion surgery is common. Optimal timing dictates that surgery occurs before respiratory function deteriorates. Cardiac effects include reduced myocardial relaxation due to dystrophy and reduced left ventricular function. Death occurs usually at around 20 years of age, often due to respiratory failure, possibly with cardiac involvement (5).

Usually bladder and bowel function and sphincter control are normal, apart from constipation associated with decreased mobility. Some autopsy studies have shown changes in the smooth muscle of the bowel wall and one clinical study has suggested delayed gastric emptying. Chewing and swallowing problems may arise in the later stages (later teens), when facial and oesophageal muscles are involved (5).

Dystrophin has been found to be present in the brain, although its function is unclear. Some intellectual or cognitive impairment is recognised in boys with DMD. The normal curve for IQ for these boys sits to the left of that for the overall population. Boys with DMD have been found to have a reading disability similar to dysphonic dyslexia (6). Emotional disturbances have also been noted (5). Functionally, DMD boys have electroencephalograph abnormalities. These findings have implications for the clinical management of boys with DMD (7).

Supported by Special Project Grant, Rocky Bay Foundation.
Rocky Bay, Western Australia
S. Leighton, GradDipDiet, Dietitian
Correspondence:
S. Leighton, Rocky Bay Inc, PO Box 53, Mosman Park, WA 6912
Email: sarahl@rockybay.org.au
Body composition and energy requirements

Boys with DMD have nutritional issues that are different from their peers. In general, these boys are of normal weight and length at birth. In the first three to four years of life, height falters and does not follow the normal pattern of growth, but stabilises after about 4 years of age. Older boys follow a normal growth curve, but height stays around 1.5 SD below normal. The absence of normal muscle tension on skeletal structures, with or without weight bearing, and poor nutrition were both thought to contribute to reduced linear growth. However, the short stature in boys with DMD now appears due to genetic factors (8).

Height is an important measure to assess growth, ideal weight, and to calculate pulmonary function, but the measurement of height may be complicated in older patients by contractures and scoliosis. For the estimation of height, an alternative anthropometric measurement has not been validated for this population. Armspan has been shown to be unreliable for those with muscular dystrophy, as elbow or shoulder contractures may be present, or they are too weak to fully extend their arms. It is possible to estimate height from a measurement of forearm segment, or ulnar segment, but this has a weaker correlation with standing height (9). Knee length has also been considered, but contractures of the flexors of the hip and knees, and a tendency to equinovarus deformity of the feet occur rapidly after loss of ambulation, similarly complicating this measurement (5).

Using measures of total body potassium, and of urinary creatinine excretion, it was calculated that boys with DMD lose muscle mass at a rate of 4% per year (10). Griffiths and Edwards (10) have proposed a set of growth percentiles for weight for boys with DMD. These are used in conjunction with the Tanner and Whitehouse longitudinal standards for height and weight (11). Height for age on the Tanner chart is used to assess which centile is appropriate to compare weight for age on the Griffiths and Edwards chart. Adding 1 kg to the ‘ideal weight’ for every year older than ten years of age accounts for the weight attributable to fibrous and fatty infiltration of muscles.

Willig et al. (12) have published a report based on data from 252 boys with DMD. There is an overall prevalence of weight for age being above the 90th centile in the seven to 13-year-age group, with up to 54% of younger DMD boys being obese. At around 13 years of age, many of these boys show an inflexion in their weight chart, stabilising between 23 to 27 kg. After 14 years of age, undernutrition becomes more prevalent, with up to 54% being underweight by 18 years of age (12). Significant rates of weight loss are found in DMD subjects from ages 17 to 21 years.

The following studies have attempted to assess the resting energy expenditure (REE), basal energy expenditure (BEE) or basal metabolic rate (BMR) in patients with DMD, and consider whether weight gain or loss is due to altered intake and/or abnormal expenditure of energy, or whether REE or BEE may be reduced as a result of decreased muscle mass.

Okada et al. (13) found that the basal metabolic rate (BMR) of patients with DMD was higher than that of controls for all ages, with the difference increasing with age, and being about 20% to 30% higher in older boys with DMD. Protein requirements were also studied. The maintenance requirement of conventional dietary protein in DMD patients was 1.26 g/kg body weight per day, about 68% higher than the normal adult requirement. Data from 267 DMD patients (aged 11 to 29 years) was used. Yearly increases in body weight were small, so a single value for maintenance requirement was made, regardless of age. Daily excretion of urinary 3-methylhistidine per unit muscle mass by DMD patients was significantly higher than for controls, indicating muscle protein breakdown. The combination of increased BMR, increased protein requirement and increased 3-methylhistidine excretion indicate that DMD is a hyper-metabolic condition. Decreased amounts of free essential amino acids, particularly branched chain amino acids, in the serum of DMD patients confirmed this.

Hankard et al. (4) in a study of 13 boys with DMD and nine age-matched controls found that in ten-year-old boys with DMD and muscle loss of 71%, REE was decreased by 13%. Differences were found between obese and non-obese boys, and it was proposed to adjust the REE for fat free mass. REE expressed per kg of fat free mass is higher in DMD boys than in controls. The fat free mass was estimated using a bioelectrical impedance analyser, but the authors advised that no method of estimating FFM has been validated for this population. Standard anthropometric measurements to estimate percentage body fat such as skinfold measurements are not appropriate for use in the DMD population, as the muscles of DMD subjects undergo extensive fibrosis and replacement by fat tissue. (14)

The Hankard et al. (4) study also measured respiratory quotient, an index of glucose to fat oxidation ratio. It appeared higher in DMD groups than controls, although statistically significant only for the non-obese DMD boys. Dietary assessment showed no differences in intake of nutrients between the groups. The higher respiratory quotient results suggest a lower utilisation of lipid in boys with DMD than in controls. As the respiratory quotient was not lower in the obese boys with DMD, these authors suggest that increased lipid stores do not enhance lipid oxidation in DMD and that low lipid utilisation may be associated with DMD at an early stage.

Okada et al. (15) state that patients with DMD are so malnourished that nutritional supplementation is crucial, due largely to the increased energy and protein requirements. Their study attempted to obtain formulae for predicting the BMR from the degree of body weight loss and the energy intake, derived from 24-hour urinary nitrogen excretion, assuming a constant (14.6%) of dietary protein-energy. The aim was to estimate energy requirements for individuals to determine the level of supplementation required. Further studies were planned by these authors to assess the effects of supplementation.

Further influences on nutrition

Assessment of height and ideal weight for an individual, management of obesity in younger boys, and supplementary feeding for underweight older boys are some of the obvious physical issues to be considered in the nutritional care of boys with DMD. Constipation may also be a problem, due to a combination of reduced mobility, dietary intake and (often) personal choice.
Psychosocial issues

Many complications arise in practice stemming from psychosocial issues that may often be the most influential. The time taken to eat as the condition progresses, having to be physically fed, difficulty with swallowing, and the time taken for toileting (requiring assistance of a carer) as a result of eating and drinking, are major considerations in the choices made throughout the day. These may particularly limit the intake of an adolescent, adding to the likelihood of further weight loss.

In the case of younger children, parents may, in view of the child’s prognosis, consider that imposing dietary regulations only adds further unnecessary burden to the child. Thus, there may be few dietary restrictions, and the child is prone to weight gain.

Steroids

Younger boys may be commenced on steroid therapy, often prednisone, which has been found to slow muscle deterioration, perhaps by the suppression of immune attack on necrotic fibres. Unlike its effect in healthy volunteers, prednisone does not increase protein degradation, but improves muscle mass indices and muscle function in DMD (14). Steroid therapy often results in weight gain (5). Steroid therapy may prolong ambulation, but there is no evidence that steroids are associated with prolonged life, or with improved cardiac or pulmonary function in DMD. Iannaccone and Nanjiama (16) consider that the risks of long-term steroid therapy are such that steroids are not recommended for routine use for DMD, and if therapy is commenced, the patient should maintain dietary energy restriction and an exercise regime.

Effects of being over- or under-weight

Carrying additional weight (as fat) places added strain on weakened muscles, including the heart and respiratory muscles as well as skeletal muscles, further limiting movement which may hasten the onset of immobility and wheelchair reliance. Reduced mobility results in decreased energy expenditure and increased likelihood of weight gain.

Hankard et al. (4) have observed no significant gain in muscle mass from being obese, and therefore consider that obesity should be considered only as a factor increasing the handicap of muscle wasting. Obesity also accentuates skeletal deformities, and complicates outcome after orthopaedic surgery.

MacDonald et al. (2), in a study of 162 boys with DMD over a period of ten years, found that the presence of obesity was unrelated to strength decline, length of wheelchair reliance, functional grade status, timed motor performance, likelihood of electrocardiographic abnormalities, pulmonary function, or age at death. These authors consider that weight control is principally important in facilitating ease of care.

Edwards et al. (17) state that obesity causes respiratory function to deteriorate, and overweight individuals are more likely to suffer post-operative chest infections. Reducing unnecessary fat will lessen the burden on weakened muscle, aid mobility and possibly improve respiratory function. They followed the progress of two boys with DMD who successfully reduced their body weight without losing muscle mass. Benefits of this included maintained physical performance, despite natural progression of the disease, including one boy becoming able to use a hand-operated wheelchair after nine years of using an electrically powered chair. Behaviour and self image improved. As a result academic performance and lifestyle opportunities improved. The study concluded that weight loss was a safe and practical way to improve mobility and self esteem.

Being underweight may reflect excessive muscle degradation. Muscle mass declines progressively in the course of DMD. However, where there is inadequate intake of nutrients, muscle will be further degraded to provide for energy. Reduced muscle mass means reduced reserve at times of illness, as well as weakened respiratory and cardiac muscles.

Specific nutrients

Although no dietary regime or supplement will alter the final outcome of muscular dystrophy, some specific nutrients have been proposed as assisting in protecting muscle from breaking down at a more rapid rate than the condition dictates.

Glutamine

Glutamine is an amino acid mainly synthesised in the muscle and is involved in many metabolic processes (13). Boys with DMD have been found to have significantly decreased whole body turnover of glutamine, which raises the question of the qualitative impact of muscle mass loss on amino acid metabolism (18).

Hankard et al. (19) examined whole body protein kinetics in a group of six nine-year-old children with DMD, and five matched controls. Intravenous infusions of leucine and glutamine were given in the post-absorptive state. Leucine is an indicator of the rate of protein degradation and oxidation. Leucine oxidation was 44% higher in DMD boys, reflecting a negative whole body leucine balance. There was a significant decrease in glutamine availability in the post-absorptive state in boys with DMD. Glutamine is proposed to be a ‘conditionally essential’ amino acid in DMD.

Boys with DMD were given oral glutamine, which was associated with a reduction in leucine release from muscle and leucine oxidation rate. There was a concomitant decrease in plasma leucine, lysine, and phenylalanine concentrations, essential amino acids whose only source in the post-absorptive state is protein degradation. Plasma insulin did not rise significantly, so the decrease in protein degradation is not likely to be due to insulin. It is unclear whether glutamine itself was responsible for the inhibitory effect on protein breakdown. Oral glutamine administration fails to stimulate protein synthesis in children with DMD unlike in healthy adults. Oral glutamine has an acute protein-sparing effect in DMD but it remains to be seen whether long-term oral glutamine administration will be beneficial in DMD (14).

A study published in 1989 on the effects of overfeeding in ten children with muscular dystrophies (six with DMD, four with congenital muscular dystrophy, found that 1000 mL of Osmolite overnight, (providing 4200kJ
and 37.2 g protein), improved nitrogen balance (more so in the DMD group) with no change in urinary 3-methylhistidine, indicating improved muscle synthesis with no change in muscle protein breakdown (20). This contrasts with the results above for glutamine alone.

Antioxidants

A Chilean study assessed the effects of vitamin E supplementation on urinary luminescence, an indicator of oxidative stress. It was found that vitamin E supplementation (400 IU/day) significantly decreases urinary luminescence in healthy children and in patients with muscular dystrophy. It was concluded that vitamin E could be useful in treatment of DMD (21).

Nitric oxide synthase (required for muscle relaxation) is associated with the sarcolemmal protein dystrophin normally, but is also absent in muscles of those with DMD. A study investigating the hypothesis that reactive oxygen species or ‘free radicals’ may contribute to the pathogenesis of DMD, investigated oxidative damage to protein in quadriceps femoris by quantifying protein carbonyl levels. The mean concentration for people with DMD was increased by 211% compared to normal subjects. This supported the hypothesis for the role of reactive oxygen species-induced protein oxidation contributing to muscle cell damage in DMD (22).

Coenzyme Q10, ubiquitin, is a naturally occurring substance that has antioxidant and membrane stabilising properties as well as contributing to respiratory chain function. Sacher et al. (23) administered coenzyme Q10 with standard medical therapy to 17 patients over four months and conclude that it enhances cardiac output (left ventricular function) in congestive heart failure. Folkers and Simonsen have conducted trials on patients with various muscular dystrophies and concluded that improved physical performance was recorded with daily supplementation of coenzyme Q10. They consider that 100 mg per day is probably too low, although effective and safe (24).

Further issues

Osteoporosis

Osteoporosis has been recognised in non-ambulatory boys with DMD. Aparicio et al. (25) have studied ten ambulatory children with DMD, aged from six to 11 years. They found weakness in the lower extremity musculature, as well as proximal femur and lumbar spine osteoporosis or osteopenia. Larson and Henderson (26) describe early development of lower extremity osteoporosis while boys are still walking, and their progression further when wheelchair bound. Hsu (27) recommends treatment by proper positioning of weakened extremities, and fracture prevention by due care of patients. Dietary contributors such as calcium and vitamin D should also be considered, especially if exposure to sunlight is limited.

Coagulation and fibrinolysis

Saito et al. (28) compared serum concentrations of creatine kinase, fibrin and fibrinogen degradation products, plasma concentration of fibrinogen, antithrombin and D-dimer in patients with various muscular dystrophies, myotonic dystrophy and spinal muscular atrophy (type 2). The findings suggested that enhanced coagulation and fibrinolysis are associated with the muscular dystrophies, but not with the other conditions. Dietary components (such as n-3 fatty acids and vitamin K) from vegetables, nuts and certain oils may modify coagulation and fibrinolysis, and so be worthy of further investigation.

Chronic inflammatory response

An absence of dystrophin does not necessarily cause necrosis. Porter et al. (29) have studied the ‘mdx mouse’, an animal model for DMD, and established a molecular signature of dystrophinopathy, with evidence that secondary mechanisms are key contributors to pathogenesis. The data provided evidence for a coordinated chronic inflammatory process. The researchers consider that this is a relatively neglected aspect of DMD, giving possibilities of new therapies. The n-3 fatty acids are known to be beneficial in reducing the inflammatory response and may also be important for membrane integrity, so effects of diet could be further explored.

Conclusion

Nutrition for boys with DMD has not been regarded as a high priority, as the course of this condition is genetically defined. However, good nutrition from an early age can contribute towards quality of life.

Difficulties arise with establishing a ‘healthy weight range’ for boys with DMD, particularly when, as teenagers, they have lost substantial amounts of muscle, but still require some padding over bones to prevent skin breakdown. Studies are required to determine an optimum weight range within which health is maintained, even though these boys may have a greater proportion of fat to muscle than for the normal population.

The psychosocial aspect of eating, family dynamics, family values, and cognitive impairment in some patients also impact on the ability of each individual to accept optimal nutrition. Given the nature of this condition, dietary choices must be such that the patient and family are satisfied with their choice, hence the value of nutrition education for families as early as possible. Cognitive differences should be considered when planning education. Regular monitoring of nutritional status from early childhood would help to establish nutrition as an important aspect of treatment, and prevent later problems related to being over- or under-weight.

It may be that certain nutritional supplements will prove useful as more studies are conducted in this area. McCrory et al. (1) have identified that studies of energy, protein, and branched chain amino acid supplementation in DMD have yielded promising but inconclusive results. They state that studies on the role of nutritional therapy to optimise the quality of life in people with DMD are urgently needed.

References


