Nutritional Problems in Patients with Duchenne Muscular Dystrophy

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ARTICLE INFO

Received: March 22, 2021
Published: March 29, 2021

Citation: Hatice Tuğçe BERBEROĞLU, Nilüfer ACAR-TEK. Nutritional Problems in Patients with Duchenne Muscular Dystrophy. Biomed J Sci & Tech Res 34(5)-2021. BJSTR. MS.ID.005610.

Keywords: Nutrition; Dietary Modification; Duchenne Muscular Dystrophy; Gastrointestinal Problems; Nutritional Problems

ABSTRACT

Duchenne muscular dystrophy (DMD) is an X-linked recessive hereditary disorder of muscles. DMD, which is a multisystemic disease, patients often experience gastrointestinal problems such as gastroesophageal reflux, constipation, dysphagia, delayed gastric motility, dental and jaw structure disorders and chewing disorders, in addition to musculoskeletal, pulmonary and heart problems. These problems, which increase with age, increase the risk of developing obesity and malnutrition and worsen the disease progression. This decreases the quality of life of patients and those who care for patients. There is no definite treatment for DMD disease. In addition to medical treatment, nutritional regulations ensure that patients receive enough daily energy, protein, various micronutrients and fluid, protect patients from obesity and malnutrition, and make dietary modifications in line with the presence of nutritional and gastrointestinal problems important. Dietary modifications such as changing the texture of foods, dividing the foods into small pieces, choosing foods with high energy content or more liquid foods should be considered as needed. If necessary, gastrostomy or enteral feeding options should also be considered. Although there are data on the benefits of dietary supplements, information on the use of these products in individuals with DMD is limited. In this review, common nutritional problems in patients with DMD, dietary modifications related to the management of these problems and nutritional therapy will be evaluated.

Introduction

Duchenne muscular dystrophy (DMD) is an X-linked recessive hereditary disorder resulting from a mutation located on chromosome Xp21 in the dystrophin gene [1-3]. DMD, affecting 1 in 3500 males, [4] is the most common congenital muscle dystrophy [4,5]. DMD is a genetic degenerative disease characterised by decreased muscle mass and function [2,6]. This degeneration starts from birth; [7] resulted pulmonary, cardiovascular, orthopaedic and nutritional complications affect the skeletal, cardiac and smooth [8,9]. Therefore, multidisciplinary clinics involving cardiologists, neurologists, dieticians, nurses, physiotherapists, geneticists, pulmonologists and primary care physicians are very crucial in diagnosing and preventing the complications and managing the progression of DMD [9-11]. Gastrointestinal disorders such as constipation, delayed gastric emptying, gastroesophageal reflux, and problems with chewing and swallowing are frequently seen in DMD [9,12-14]. Nutrition therapy and dietary modifications ameliorate disease progression by decreasing complications [13,14]. In this review, we will assess the nutritional problems frequently seen in patients with DMD, dietary modifications related to the management of these problems and nutrition therapy.

Duchenne Muscular Dystrophy and Nutritional Problems

Gastrointestinal and nutritional complications, which are common in neuromuscular diseases, [12,13] increase with age [12]. Increased or decreased body weight, mandibular contracture, [15] gastroesophageal reflux, [9,13] delayed gastric emptying, constipation, [9] chewing disorders, choking episodes, [9,13]
Examples of Foods

Chewing likely required: Dysphagia Diet. Soft foods, requires more chewing. Mechanical altered, requires some chewing. Soft foods, requires more chewing. Regular. Chewing likely required. All foods allowed.

Description of Texture | Examples of Foods
--- | ---
Level 1 | Purees, consistent texture throughout, requires no chewing. Stage 1 and 2 baby foods, applesauce, yogurt without pieces of fruit.
Level 2 | Mechanical altered, requires some chewing. Oatmeal, mashed potatoes, banana, refried beans, canned fruits and tender-cooked vegetables.
Level 3 | Soft foods, requires more chewing. Chopped meats and fish, breads, most fruits without skins or seeds.

Management of Nutritional Problems

In recent years, there has been an increase in studies on nutritional difficulties in patients with DMD, demonstrating an increased interest in the assessment and management of nutritional problems of individuals with neuromuscular diseases [9,11-13,16,20,21,37]. A multidisciplinary approach, which includes dieticians, speech therapists, neurologists and pneumologists, is required for the management of eating disorders in patients [13,16]. Regular assessment of dysphagia is very important. It is important to examine if there are difficulties in swallowing food, if food is adhering to the throat; it is also important to assess the average time to eat and the effects of food on quality of life [11,38]. In patients with dysphagia that do not aspirate, it is beneficial to divide food it into small pieces [13,16,18] or provide liquid foods [13,18]. In addition, water consumption during and after meals has been shown to reduce swallowing problems and remove oropharyngeal food residues [21]. Thickening agents have also been used for many years to prevent dysphagia in patients with swallowing difficulties [37]. However, previous studies have shown that these thickeners are not suitable for patients with DMD and other neuromuscular diseases [37,39] because thickened liquid and solid foods increase oral phase problems and pharyngeal residue accumulation [37]. Food texture is classified by 4 main categories of viscosity which can be altered to facilitate swallowing. Table 1 shows dysphagia diet and sample foods at all levels [9,40].

Table 1: Dysphagia Diet.

| Level | Description of Texture | Examples of Foods |
|---|---|---|
| 1 | Purees, consistent texture throughout, requires no chewing | Stage 1 and 2 baby foods, applesauce, yogurt without pieces of fruit |
| 2 | Mechanical altered, requires some chewing | Oatmeal, mashed potatoes, banana, refried beans, canned fruits and tender-cooked vegetables |
| 3 | Soft foods, requires more chewing | Chopped meats and fish, breads, most fruits without skins or seeds |
| Regular | Chewing likely required | All foods allowed |

Obesity increases the risk of glucose intolerance and promotes disease progression by increasing the burden on weakened muscles [18,30]. Other complications of obesity include insulin resistance, dyslipidemia, hypertension, obstructive sleep apnoea, [9,31] impaired pulmonary and cardiac functions [9,12,16] and hypercapnia caused by increased carbon dioxide production as a result of excessive nutrition [5,32,33]. Due to decreased appetite, difficulty in swallowing and chewing and digestive problems, the patients are at risk of malnutrition, [18] increased muscle loss, [5,34] pressure sores and decreased immunity [5,35,36]. Therefore, considering all these problems, complications caused by malnutrition reduce the quality of life of patients with DMD and the caregivers [8,12,18,21].
In patients with severe swallowing disorders or decreased body weight as a result of malnutrition, a gastrostomy tube and surgical intervention should be considered [13,18,37]. In case of aspiration, percutaneous endoscopic gastrostomy should be considered with the complete prohibition of oral food intake [37]. At the same time, the presence of malocclusion or macroglossi or both, which are frequently seen in patients with DMD, should not be ignored [37,41,42] because these problems reduce tongue movement and affect the passage of food into the pharynx [37,43]. Dietary modifications should be made according to tongue pressure levels of patients. For example, patients with low tongue pressure should eat a less solid diet [37,44]. In addition, it is recommended to consume frequent and small amounts of energy-dense food to reduce the time and effort spent on eating. Lastly, it is recommended to rinse the throat with water after each meal [37,45]. Delayed gastric emptying in DMD patients is significantly increased compared with that in healthy individuals; it worsens with the progression of the disease [46]. Delayed gastric emptying slows down access of nutrients to the small intestine causing malnutrition [9,46]. Gastroesophageal reflux increases the risk of aspiration [12]. Appropriate treatment options include dietary modification, pharmacological treatment and post-pyloric feeding via a gastrojejunal feeding tube [11].

Gastroesophageal reflux is another gastrointestinal problem of patients with DMD. It is recommended that individuals with reflux symptoms consume less food but more frequently [11]. Treatment of constipation is particularly important in malnourished patients [9]. Nutrition and drug therapy should be applied according to the causes and severity of constipation in these individuals [9,47]. Complementary and alternative medicines are often used to ameliorate symptoms in these individuals. Although these types of treatments have been beneficial in some cases, further research is needed to confirm their safety and efficacy [9]. Adequate fluid and fibre consumption can prevent or treat constipation [12]. Fibre requirements of males at the age of 4-8, 9-13 and 14-18 are 25 g/day, 31 g/day and 38 g/day, respectively [9]. To prevent dental health problems, the patients should avoid excessive consumption of sugary or acidic food and beverages and brush their teeth regularly [18]. Although nutritional complications are common in individuals with DMD, they are directly linked to the progression of the disease and quality of life. To improve the quality of life of these patients, a multidisciplinary treatment approach is needed that combines understanding the factors that adversely affect the nutritional status of the patient, anthropometric measurements and dietary modifications.

### Nutritional Approach in Duchenne Muscular Dystrophy

Nutritional imbalances of individuals with DMD adversely affect respiratory, skeletal muscle and cardiac systems [11]. However, an appropriate nutrition programme can improve the quality of life of patients with diagnosed with neuromuscular disease and their family members [20]. The aim of nutritional therapy is to prevent obesity and malnutrition by evaluating body weight and height regularly [11]. As the disease progresses, a dietician should be consulted to prevent obesity and malnutrition and to administer drug or non-drug treatments by monitoring nutrition and the gastrointestinal system [20]. Because there are no recommendations for daily energy and protein intakes for individuals with DMD, there is a need to develop nutritional guidelines according to the different needs of patients at different stages of the disease. For this purpose, studies involving metabolic results of distroptatology and disease progression are needed that can clearly explain the effect of changing energy and nutrient requirements [48]. If patients unintentionally lose >10% of their body weight in 1 year; it is recommended to increase nutrients and energies [37]. It is very important for individuals with DMD to ensure adequate intake of protein, calcium, vitamin D and fluids and both soluble and insoluble forms of fibre [49,50]. In a review published in 2018 by Birnkrant et al., it was shown that 45-65% of total energy intake should be obtained from carbohydrates, 20-35% from fats and 10-35% from proteins. Acceptable ranges for children and adolescents are similar to adults [11,51].

### Protein Requirement

Although there is very little data in the literature about the amount of protein that individuals should consume, the minimum amount of protein to be taken should be adjusted according to DRI recommendations for age. It is recommended that 10%-30% of total energy consumed in individuals between the ages of 4–18 years come from protein [9,52]. Table 2 summarizes energy and protein intake recommendations for each age group [9]. It has been reported that individuals of age 4–13, 14–18 and 19 years should consume 0.95, 0.85 and 0.80g/kg weight/day protein, respectively [11]. The effects of this amount on disease pathology in mouse models are shown to be uncertain [53,54]. Some studies report that high protein diets do not have any positive effect [18]. Limited findings on the positive effects of additional protein intake on the disease suggest that additional protein intake is not necessary in these patients [9,12,53].
Table 2: Estimated Energy and Protein Requirements for Males 3-18 Years.

| Age (Years) | Dietary Reference Intake-Energy | Dietary Reference Intake-Protein |
|-------------|--------------------------------|----------------------------------|
|             | Basal Metabolic Rate (kcal/kg/d) | kcal/d | kcal/kg/d | g/d | g/kg/day |
| 3           | 57                             | 1020   | 85        | 13  | 1.08     |
| 4-5         | 48                             | 1402   | 70        | 19  | 0.95     |
| 6-7         | 48                             | 1279   | 64        | 19  | 0.95     |
| 8           | 48                             | 1186   | 59        | 19  | 0.95     |
| 9-11        | 36                             | 1756   | 49        | 34  | 0.94     |
| 12-13       | 36                             | 1599   | 44        | 34  | 0.94     |
| 14-16       | 28                             | 2385   | 39        | 52  | 0.85     |
| 17-18       | 28                             | 2230   | 37        | 52  | 0.85     |
| >18         | 28                             | 2550   | 36        | 56  | 0.80     |

**Micronutrients**

Although little is known about the daily micronutrient requirements for patients with DMD, it is known that vitamin D and calcium are the most important nutrients during corticosteroid treatment in patients [16]. Canalis, et al. [55] reported that glucocorticoids cause osteoporosis by suppressing bone formation and increasing bone resorption. Decreased physical activity has a negative effect on bone health, increasing the risk of fractures in these individuals [56]. In a case-control study by Söderpalm et al. [56] serum 25 (OH) D vitamin levels were compared in 24 patients with DMD and 24 healthy individuals, most of whom received prednisone treatment. It was shown that serum vitamin D levels, bone mineral density and bone turnover were significantly lower in DMD patients compared with healthy subjects even though food consumption records showed that they both received sufficient amounts of vitamin D and calcium. Therefore, it is thought that either the vitamin D and calcium requirements for individuals diagnosed with DMD should be increased or there is a different mechanism that causes vitamin D deficiency in DMD patients. Recent studies have shown that children with DMD may have low serum 25 (OH) D levels and poor bone health at the time of diagnosis, even before initiating steroid therapy [57,58]. In addition, increased bone turnover and decreased serum 25 (OH) D levels were found in DMD patients with or without steroid treatment. In a study by Biggar, et al. [59] patients receiving corticosteroid therapy were recommended to receive 750 mg calcium and 1000 mg IU vitamin D supplementation. In another study, it was emphasised that elemental calcium intake should vary with age: 1000 mg/day between 4–8 years, 1300 mg/day between 9–18 years and 1000 mg/day after 18 years [60]. In addition to consuming foods rich in calcium and vitamin D, nutritional supplements can also be used to ensure adequate calcium and vitamin D intake [9]. However, there is little data in the literature about which type and what doses should be consumed [18].

**Fluid Requirement**

There is limited information in the literature about the amount of fluid consumed by individuals with neuromuscular disease; however, adequate fluid consumption is recommended to help prevent constipation [12]. Fluid requirements of individuals vary with physical activity, age and weather, but patients are recommended to take 2 L of fluid daily [49]. In a review, it is reported that the recommended fluid consumption may vary according to body weight in addition to age. It is recommended to intake 1.2 L between ages 4–8 years, 1.8 L between ages 9–13 years, 2.6 L between ages 14–18 years and 3.0 L for those older than 19 years old. The Holliday-Segar method, which determines fluid requirement based on body weight, is shown in Table 3 [11,61].

**Various Nutritional Supplements**

It is estimated that the use of alternative and complementary medicine such as nutritional supplements for the management of chronic diseases worldwide varies between 6% and 65% in adults [62]. There are also studies showing the use of these nutritional supplements by paediatric populations who have chronic disease or disability [63,64]. In two Canadian studies, the frequency of use of alternative and complementary medicine in the paediatric population with neuromuscular disease and DMD were reported to be 30% [65] and 20%, [66] respectively. The results of the meta-analysis of Nabukera, et al. [67] showed that the use of these supplements is quite common in patients with DMD and Becker Muscular Dystrophy. So far, studies have been conducted investigating the effects of many different nutrients on
the progression of the disease. These include n-3 fatty acids, [68] leucine, [69] vitamin D[29] L-carnitine, [70] Coenzyme Q10, [71] taurine, [72] green tea extract, [73] curcumin [74] and resveratrol [75]. However, data on the benefits of nutritional supplements are limited and contradictory. In addition, there are no standardised guidelines for the doses of these nutritional supplements. [18]. Although nutritional supplements may have potential positive effects, they can be harmful if taken at high doses or with other drugs because there is a possibility for drug interaction[18].

Conclusion

DMD is a multisystemic disease that progresses with the catabolic processes of the body and causes skeletal, cardiac, pulmonary, gastrointestinal system and nutritional problems. These problems include obesity, malnutrition, chewing and swallowing disorders, tooth and jaw structure disorders, constipation, delayed gastric mobility and gastroesophageal reflux. These problems significantly decrease the quality of life in these patients by deteriorating their nutritional status and causing the disease progression. Recent studies have emphasised the need to adopt a multidisciplinary approach in the management of nutritional difficulties and gastrointestinal problems that involves speech therapists, dieticians, neurologists and pneumologists. Anthropometric measurements and body composition should be evaluated regularly in these patients to determine their required energy intake. In addition, dietary modifications should be considered such as changing the food texture, dividing the foods into small pieces, preferring foods with high energy content or consuming more fluids. Additionally, when necessary, the use of gastrostomy tube or enteral nutrition products should be considered. Although nutritional supplements may provide some benefit, there is limited information on the effective use of nutritional supplements for patients with DMD, which warrants further studies. In summary, it is expected that proper patient evaluation and adoption of a tailored approach will improve the quality of life of patients and their caregivers.

Contributors

Both authors wrote sections, controlled English grammar, spelling, approved the final manuscript and followed journal guidelines.

Disclosure Statement

No potential conflict of interest was reported by the authors.

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