DIAGNOSIS AND MANAGEMENT OF DUCHENNE MUSCULAR DYSTROPHY

Part 2: Respiratory, cardiac, bone health and orthopaedic management

OVERVIEW

Duchenne muscular dystrophy (DMD) is a lethal X-linked recessive neuromuscular disorder caused by mutations in the dystrophin gene, leading to progressive muscular damage and degeneration.

The 'DMD care considerations' were first published in 2010. They have been updated to reflect several important developments, including the improved survival of patients with DMD, evolving diagnostic and therapeutic approaches, an increasing emphasis on quality of life and psychosocial management and experience with existing therapies, and emerging therapies.

Part 2 contains the latest care considerations for respiratory, cardiac, bone health and osteoporosis, and orthopaedic and surgical management, plus guidance on cardiac management for female carriers of a disease-causing mutation.

RESPIRATORY MANAGEMENT

Respiratory complications are a major cause of morbidity and mortality in people with DMD. Complications include respiratory muscle fatigue, mucus plugging, atelectasis, pneumonia and respiratory failure.

Anticipatory management includes monitoring of respiratory muscle function, lung volume recruitment, assisted coughing, nocturnally assisted ventilation and subsequent daytime ventilation. These core therapies have shown to decrease respiratory complications, improve quality of life and prolong survival.

Serial monitoring of pulmonary function (forced vital capacity, FVC) is critical for respiratory management. Individuals with DMD should receive yearly immunisation with the inactivated influenza vaccine and pneumococcal vaccines.

Higher pulmonary function thresholds (that is, milder respiratory impairment; FVC <50% predicted, PCF <270 L/min, or MEP <60 cm H_2O) are recommended for initiation of assisted coughing and assisted ventilation, compared to the 2010 care considerations

CARDIAC MANAGEMENT

Cardiovascular complications are also a major cause of morbidity and mortality in people with DMD. Dystrophin deficiency leads to cardiomyopathy, and as the myocardium fails to meet physiological demands, clinical heart failure and cardiac arrhythmias may follow. In non-ambulatory individuals, signs and symptoms of heart failure are often subtle and overlooked, making a proactive strategy of early diagnosis and treatment essential.

Cardiovascular assessment (cardiac medical history, physical examination, electrocardiogram, non-invasive imaging) is recommended annually, or more frequently if the patient is symptomatic.

First-line therapy comprises angiotensin-converting enzyme (ACE) or angiotensin receptor blockers (ARBs), where the choice of agent and dose is at the discretion of the cardiologist. Ventricular dysfunction typically prompts ß-adrenergic blockade. Severe left ventricular dysfunction may necessitate thromboembolism prevention. Holter monitoring and standard antiarrhythmic medications are used to manage cardiac arrhythmias. Implantable cardioverter defibrillators are used in individuals with an ejection fraction of <35%.

Female carriers are also at risk of cardiomyopathy and should be assessed every 3–5 years if asymptomatic. If symptomatic or imaging positive increase assessment frequency on the basis of cardiologist recommendation

BONE HEALTH AND OSTEOPOROSIS MANAGEMENT

Glucocorticoid therapy and progressive myopathy are both key risk factors for reduced bone strength. Boys with glucocorticoid-treated DMD frequently develop osteoporosis, which manifests as low-trauma vertebral or long-bone fractures. While vertebral fractures are often asymptomatic, if left untreated they may lead to chronic back pain and spine deformity. Leg fractures can cause premature permanent loss of ambulation.

An important update is that bone health monitoring in children no longer focuses on bone mineral density (BMD), but on detection of the earliest signs of bone fragility. In the current care considerations, a baseline spine radiograph for vertebral fracture detection is recommended in all patients, with intermittent follow-up radiographs.

Given the risk for future fractures, treatment of asymptomatic moderate and severe vertebral fractures is now recommended. Intravenous bisphosphonates are recommended as first-line treatment for osteoporosis in patients with DMD, following a published regimen that includes regular safety and efficacy monitoring. Patients should be referred to an expert in osteoporosis management for treatment.

ORTHOPAEDIC MANAGEMENT

The aims of musculoskeletal care are to maintain motor function for as long as possible, minimise joint contractures, maintain a straight spine and promote bone health.

Range of motion should be assessed every 6 months. The spine should be examined at least annually in ambulatory patients, increasing to every 6 months in non-ambulatory patients. Radiographic assessment should be carried out if a curve is observed or visual inspection is difficult, for patients with known progressive scoliosis, or when a patient becomes non-ambulatory. A curve of 20° or more should warrant involvement of an orthopaedic surgeon. Patients treated with glucocorticoids have been shown to have milder spinal curvatures and less frequent need for spinal surgeries than untreated boys.

Individuals with DMD should be educated on a home stretching programme, initially focusing on the ankles, knees and hips. Ankle-foot orthoses may be indicated in some patients; spinal orthoses are not recommended. Anticipatory fracture prevention guidance should be provided to families, and healthcare providers and families should be aware of fat embolism syndrome.

SURGICAL CONSIDERATIONS

A cardiologist and respiratory physician should be consulted before all surgical procedures. Use of cough techniques and non-invasive ventilation form part of respiratory care. Anaesthetists should be aware that individuals with DMD are at risk of cardiac and respiratory decompensation during and after surgery. Patients with DMD are at risk of developing rhabdomyolysis with inhalational anaesthetics or when given suxamethonium chloride. Total intravenous anaesthesia is strongly recommended. Depolarising muscle relaxants, such as suxamethonium chloride, are absolutely contraindicated due to risk of fatal reactions.

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Developed and funded by PTC Therapeutics.
This material is intended for healthcare professionals only.
Date of preparation: October 2020 | GL-DMD-0274

MEP, maximum expiratory pressure; PCF, peak cough flow. **Reference:** Birnkrant DJ, *et al. Lancet Neurol.* 2018;17:347–361.