Indian Association of Physical Medicine & Rehabilitation

CLINICAL PRACTISE GUIDELINES FOR DUCHENNE MUSCULAR DYSTROPHY (DMD) FOR PHYSIATRIST IN DIFFERENT SETTINGS; 2018

DISCLAIMER

The intent of the write up "**CLINICAL PRACTISE GUIDELINES FOR DUCHENNE MUSCULAR DYSTROPHY(DMD) FOR PHYSIATRIST IN DIFFERENT SETTINGS "** is not an alternative to any books nor to replace the assessment and treatment procedures in the rehabilitation of children with DMD in different institutions, advance research settings, private and government medical colleges.

This is an attempt to make standard guidelines about complete rehabilitation management of DMD in view of Indian scenario and to help the students, interns, senior residents, physiatrists and related medical specialities.

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Definition:

Duchenne muscular dystrophy (DMD) is a rare genetic X-linked recessive disorder caused by mutation in the gene encoding dystrophin, a protein expressed in the skeletal, respiratory and cardiac muscles. The illness affects proximal muscle groups in males resulting in severe muscular dystrophy. There is variability in onset from 2 to 6 years. It is progressive in nature with steady decline in strength of the skeletal and later cardiac muscles with reduced lifespan

1. Etio-pathogenesis:

Mutations in Dystrophin gene (mainly deletions, DMD; locus Xp21.2)

Dystrophin deficiency at the plasma membrane of muscle fibers disrupts the membrane cytoskeleton and leads to the secondary loss of other components of the muscle cytoskeleton. The primary consequence of the cytoskeleton abnormalities is membrane instability, leading to membrane injury from mechanical stresses, transient breaches of the membrane, and membrane leakage (Image 1).

Chronic dystrophic myopathy is characterized by aggressive fibrotic replacement of the dead muscle fibers and eventual failure to regenerate followed by complete absence of dystrophin protein.

2. Clinical Presentations:

- Child less than 15 years of age
- Careful history reveals mild delay in motor milestones
- Parents noticing gradual onset of difficulty in walking, climbing stairs & getting up from floor, accompanied by pain & frequent falls.
- Positive family history of other relative, male siblings affected.
- Symmetrical weakness of proximal girdle muscles
- Pseudohypertrophy of calf muscles.
- Posterior axillary depression sign: Seen in advanced stage of disease. Prominent deltoid superolaterally and infraspinatus inferomedially causes posterior axillary depression (Image 2)
- Walking on toes (Equinus Deformity)
- Increase in lordosis of lumbar spine.
- Hypotonia
- When the child is lifted up holding the axilla the child may slip down due to pectoral muscle weakness.
- Positive Gower 'sign
- Tightness and/or postural contractures setting in ankles, knee, elbows, wrists, hips and spine.

- Children also frequently have varying degrees of mild cognitive impairment or global developmental delay.

- **Myopathic gait pattern: DMD affected children's walk with anterior pelvic tilt and lumbar lordosis** (compensate for hip extensor weakness)**. They have decreasing stance-phase knee flexion and plantar flexion** (compensate for knee extensor weakness). **Hip abductors weakness** (tendency toward lateral pelvic tilt and pelvic drop of the swing-phase side).

3. Complications of DMD

A. **Scoliosis:** The reported prevalence of scoliosis in DMD varies from 33% to 100%. Fifty percent of DMD patients acquire scoliosis between ages 12 and I5, corresponding to the adolescent growth spurt

B. **Contractures**: Significant joint contractures have been found in nearly all DMD children older than age 13. The most common contractures include **ankle plantar flexion and inversion,** knee flexion, hip flexion, iliotibial band, elbow flexion, and wrist flexion contractures.

C. **Respiratory complications**: most common is chest infections -Patients with DMD typically show a **linear decline in percent predicted FVC between 10 and 20 years of age**.

D. **Cardiac complications**: **Cardiomyopathy** is usually noted after 10 years of age and occurs in **nearly all patients by age 18**. Cardiac evaluation revels **A loud pulmonic component of the second heart sound suggests pulmonary hypertension** in patients with restrictive pulmonary compromise. **ECG findings**- **Q waves** in the lateral leads are **the first abnormalities to appear**, followed by elevated ST segments and poor R wave progression, increased R/S ratio, and resting tachycardia and conduction defects. **Ventricular ectopy** is a known complication

of the cardiomyopathy in DMD that probably explains the **observed cases of sudden death**. The onset of **systolic dysfunction** noted by echocardiography is associated with a **poor prognosis**. Death has been attributed to **congestive heart failure** in as many as **40-50%**

E. **Obesity:** It is a substantial problem in DMD, subsequent to the loss of independent ambulation.

F. **Mental retardation:** The **dystrophin isoform** is present in the brain which explains the **reduced IQ in DMD**.

4. Relevant Investigations:

A. Blood:

Serum creatine kinase is a useful screening test: CPK elevation during the active phase of the disease. Early in the disease process, CPK levels are 50-300 times greater than normal levels, but the levels tend to decrease as the muscle mass decreases.

B. Electro-diagnostic Test

Helps diagnose the pathology of muscle, can guide site of muscle biopsy. Normal nerve conduction velocity.

On needle EMG; Presence of abnormal spontaneous activity. (Positive sharp wave/fibrillation potentials with **Low amplitude, often polyphasic, brief duration potentials** with early recruitment)

C. Muscle biopsy:

Two techniques

I. open biopsy

II. needle biopsy

Selection of the muscle depends on clinical EMG evaluations.

For routine diagnostic studies; **Vastus lateralis** muscle in the lower extremity and **triceps or biceps** in the upper extremity When proximal muscles are severely affected **Extensor carpi radialis and Tibialis anterior** can be used. Muscle biopsy demonstrates degeneration, regeneration, isolated "opaque"

hypertrophic fibers and significant replacement of muscle by fat and connective tissue.

D. **Immunoblotting and immunostaining:** Immunoblotting of a muscle sample provides information about **amounts of specific muscle protein**, such as **dystrophin** or other structural proteins

E. **Ultrasound of muscles**: showing fibrosis in muscles.

F. **Genetic Analysis:** deletions/duplications (the most common form of mutations, seen in about 70 to 80 percent of cases)

5. Rehabilitation Assessment:

- Manual Muscle Test using MRC scale:
- Chest expansion using measuring tape across the chest at the level of the nipples in the 4th Intercostals space with scapulae elevated.
- Clinical vital capacity asking to blow and feel the air from distance from mouth.
- Ability to count numbers without break
- Active and passive range of motion of all joints of both upper & lower limbs
- Look for contractures in ankles, knees, hips, shoulders, elbows and wrists.
- Power of crutch and wheel chair propulsion muscles.
- Spine –Scoliosis mainly "C" curve.
- Early gait examination to look for biomechanical abnormalities

6. Management:

Quick Functional Assessment and Grading and planning rehabilitation program

A. Can walk with mild equinus and minimal lordosis:

I. Daily Exercises diary to be maintained: Needs active exercise program to maintain the strength, comprising of gravity assisted exercises in the beginning and gravity eliminated exercises with slings for the weak muscles. Exercises against gravity to be restricted once the child showing motor weakness in affected muscles.

II. AFO (ankle foot orthosis) to be worn most of the time while walking as long as the equinus deformity is dynamic. AFO to be wear for two hours a day during sitting time and for 3hours during sleeping time to prevent equinus.

III. Prolonged standing during leisure hours to improve tone in the postural muscle. To fix a back support in the chair with lumbar pad to keep the lumbar spine in extension to lock the facets which may in some children delay onset of scoliosis.

IV. Exercises to improve breathing especially to use more diaphragmatic breathing.

V. Schooling and social participation to be maintained

VI. Occupational therapy to maintain and modify ADL functions with minimal energy expenditure.

VII. Basic pulmonary function tests and periodic cardiac evaluation with ECG and Echo cardiogram.

B. Can walk with moderate equinus and moderate lordosis and can climb stairs with support

I. In addition to the program in grade 1, standing for a long time near the window to observe the surroundings is important for standing endurance and for the bone mineral density.

II. Walking aids can be prescribed depending on the environmental need.

III. Gradual inclusion of wheel chair activities so that the child can master the skills. Respiratory exercises are very important during this phase.

IV. Basic Pulmonary Function test to be done during follow up visits at regular intervals

V. Hydrotherapy to be done under supervision to maintain the muscle function.

VI. Avoid eccentric exercises like coming down the stairs or ramps.

VII. Orthosis to prevent contractures should be worn during rest time.

C. Walk with support but cannot climb stairs.

I. The use of orthosis to maintain verticality and assisted ambulation to tackle the contractures at earliest will be beneficial.

II. Respiratory evaluation should be done more frequently.

III. Assessment of nutritional status and spacing of meals to avoid accumulation of fat.

IV. Therapy modalities to prevent contractures, to maintain the possible erect posture and muscle function.

V. Occupational therapy to improve and maintain function and assistive aids for independence.

VI. Encourage inspiration exercise.

D. Can walk few steps with aids and maximal physical assistance.

I. Child may lose functional walking. Light weight manually propelled wheelchair will be helpful, but children should be discouraged to use the ankle and foot for propulsion resulting in early onset of contractures.

II. Since there is progressive weakness of proximal muscle groups proper stabilization of pelvis will be difficult. A customized seating system with both ischial tuberosities parallel to each other and lateral uprights to keep the spine

in vertical alignment will help to improve the posture of spine. This will reduce the energy required to maintain the posture and better breathing.

III. Ankle foot orthosis to be worn while the child is in wheel chair.

IV. Occupational therapist should make adaptation in the utensils, dressing to make the child as much functionally possible.

V. Pulmonary functions test and supplement periodical oxygen therapy will improve the sleep and functional activities.

VI. Home ventilators can be considered when children feel headache in the morning due to slow accumulation of CO2 in the night.

E. Unable to use manually propelled chair and can use powered heel chair (if available), otherwise bedridden and sits with maximum physical assistance.

I. Postural management

II. Passive movements and stretches for all joints, preferably using gravity to stretch to avoid pain

III. Encourage regular changes in position perhaps with an advanced powered wheelchair (lie to stand functions).

IV. To recline periodically to avoid load on the spine and neck muscles.

V. Pressure areas like spine, heels elbows to be examined daily for skin breakdown and measures to prevent pressure sore.

VI. Hip pain due to scoliosis or hip subluxations to be tackled.

VII. Passive head support should be given to assist in feeding and during movements.

F. Bed Ridden

I. Totally dependent for all care, only finger movements will be present
II. Nutritional issue like weight loss due to inability sallow Chest infections, hypoxia, pain due to contractures and deformities.
III. Home ventilation if available.
IV. Passive movements and regular positioning to relieve pain and pressure
V. Cough augmentation and chest clearing techniques if tolerated
VI. Ventilation used more frequently at this stage.
VII. Regular auscultation and pulmonary care.
VIII. Splints will give more pain. Occasionally collar is required

G. Palliative care

I. It is appropriate to relieve or prevent suffering and to improve quality of life in patients who have DMD, as

needed. In addition to pain management, home based ventilatory support, nursing care, palliative care teams might also be able to provide emotional support, assist families in clarifying treatment goals and making difficult medical decisions, facilitate communication between families and medical teams, and address issues related to grief, loss, and bereavement. Engaging palliative care could ease the transition process by providing families the support systems they need to accept and acknowledge death and allow them instead to focus on affirmation of life through patient education and informed decision-making about future life and medical choices.

H. Psychosocial management

I. The medical care of a patient who has DMD and his family is not complete without support for their psychosocial wellbeing. For many parents, the stress caused by the psychosocial problems of their child exceeds the stress associated with the physical aspects of the disease. Needs vary with the age of the patient and stage of disease. Peer counselling, becoming a member in DMD parental group will reduce the stress.

II. Some specific areas of risk are of particular concern like difficulties in social functioning, physical limitations resulting in social isolation, social withdrawal, and reduced access to social activities, the pattern of speech and language deficits, including those in language development, short-term verbal memory, and phonological processing, as well as cognitive delays, including impaired intelligence and specific learning

disorders. There is also increased risk for neurobehavioural and neurodevelopmental disorders, depression and anxiety. Parents with the help of local friends arrange for home learning.

III. Crucial times to consider psychosocial assessments include the time around diagnosis, before entering school, and after a change in function. Assessments are targeted at the areas of emotional adjustment and coping, neurocognitive functioning, speech and language development, the possible presence of autism spectrum disorders, and social support. Routine screening of psychosocial wellbeing in the parents, and siblings is also necessary. Participating in social meeting through multi media, playing brain stimulating games with video technology and Virtual reality will keep the neurons in brain active.

IV. Among interventions, of importance to patient/family psychosocial health is the designation of a health care provider who can serve as a point of contact for families and who has sufficient knowledge and background in neuromuscular disorders to be able to meet the family's information needs, provide psychosocial intervention to address their understanding of and attitude toward the disease, as well as burden of dealing with it, and to help them develop their coping skills and meet their children's and their own needs. Proactive intervention to help families and patients avoid the social problems and social isolation that occur in the context of DMD is necessary.

V. Development of an individual education plan for all children with DMD in collaboration with their parents

and schools is necessary to address potential learning problems. In addition, this will help with modification of activities that might otherwise prove harmful to the child's muscles (eg, physical education) or might lead to reduced energy/fatigue (eg, walking long distances to class) or safety (eg, playground activities) and accessibility issues. Promoting patient independence and involvement in decision making is also necessary.

VI. Psychopharmacological interventions should be considered for the treatment of moderate to severe psychiatric symptoms as part of a multimodal treatment plan that includes appropriate psychotherapies and educational interventions.

I. Nutrition management:

I. Proper calories with spreading the meal as eight meals a day to avoid increase in body weight.

II. Patients should be routinely weighed for excess weight gain or weight loss requiring dietetic evaluation.

III. Chronic treatment with corticosteroids increases the risk of becoming overweight, insulin resistance, and type 2 diabetes mellitus.

IV. If excess weight gain: Glucose metabolism should be evaluated with paired glucose and insulin levels, glycosylated haemoglobin levels, and the oral glucose tolerance test.

V. Muscle weakness can cause dysphagia, gastrointestinal problems (i.e., constipation, delayed gastric emptying), prolonged mealtime, and dependent feeding.

VI. Respiratory failure in the late stage of the disease can cause increased energy requirements. Under nutrition can deteriorate respiratory function and immunological responses with increased risk of chest infections. Early introduction of anitibiotic therapy will lessen the respiratory infections

J. Surgical management of contractures and scoliosis

I. Contracture release surgery can be done in view of potential capacity of ambulation of child and anesthetic risk. Proper parental counseling and wise decision in view of potential ambulation is required.

II. Childrens with DMD they are susceptible to perioperative respiratory, cardiac and other complications, such as rhabdomyolysis. Inhalational anaesthetic agents have been implicated as a cause of acute rhabdomyolysis that can resemble malignant hyperthermia (MH). However, immediate conversion to total **intravenous anesthesia** (TIVA) and a **clean anesthesia machine** is recommended, and the child should be **carefully monitored for signs of rhabdomyolysis** (serum K+ level) because, even if the risk is low, its occurrence is unpredictable.

CONCLUSION:

Progressive Muscular diseases produce a big impact on the patient and the family members. The unavailability of cure makes the patient to seek multiple physicians and alternative therapies. As a physiatrist our main objective is to improve and maintain the function for the affected child as much and as long as possible. The prolonged care required in treating DMD patients will have huge financial problem for the patients. Physiatrists should take a lead role in training the parents/ caregivers for home management.

APPENDIX:

SCALES USED FOR INTERVENTIONS, OFFICIAL AND RESERCH PURPOSES

- Wee FIM (Functional Independent Measure)
- ICF scale
- Functional Mobility scales.

The common functional scales to rate the grade of disease severity are the

- Brooke Scale and
- Vignos Scale.

The Brooke scale was designed to assess the **upper extremity function**. The grades of the Brooke scale range from 1 to 6; 1 means that the subject can elevate their arms full range to the head with the arms straight; while 2 means that the shoulder strength is insufficient to elevate their arms and the subject needs to flex the elbow to elevate the arms; in grades 3 and 4, the subject is unable to elevate the shoulders but can raise hands to the mouth with or without weight respectively; grade 5 refers to the subject being unable to raise hands to the mouth and only some hand movement exists, while grade 6 refers to no useful function of hands

Grade	Description
1.	Starting with arms at the sides, the patient can abduct the arms in a full circle until they touch above the head
2.	Can raise arms above head only by flexing the elbow (shortening the circumference of the movement) or using accessory muscles
3.	Cannot raise hands above head, but can raise an 8-oz glass of water to the mouth
4.	Can raise hands to the mouth, but cannot raise an 8-oz glass of water to the mouth
5.	Cannot raise hands to the mouth, but can use hands to hold a pen or pick up pennies from the table
6.	Cannot raise hands to the mouth and has no useful function of hands

Table 1: Brooke scale

The Vignos scale was designed to assess the **lower extremity function**.

The grades of the Vignos scale range from 1 to 10; 1 means that the subject can walk and climb stairs without assistance; 2 and 3 means that the strength is insufficient to walk upstairs without assistance as they need to use a rail for climbing stairs (grade 2: in a normal speed; grade 3: slowly) grades 4 and 5 refer to subjects still having the ability to walk unassisted but unable to climb stairs (grade 4 also can rise from a chair but grade 5 cannot); grades 6 to 8 refer to patients using the long leg brace for walking or standing (grade 6: walk without assistance; grade 7: walk with assistance for balance; grade 8: cannot walk, only for standing); grade 9 refers to the subject being unable to stand, but can sit in a wheelchair; and the final grade 10 refers to the subject being confined to a bed

Grade	Description
1.	Walks and climbs stairs without assistance
2.	Walks and climbs stair with aid of railing
3.	Walks and climbs stairs slowly with aid of railing (over 25seconds for eight standard steps)
4.	Walks unassisted and rises from chair but cannot climb stairs
5.	Walks unassisted but cannot rise from chair or climb stairs
6.	Walks only with assistance or walks independently with long leg braces
7.	Walks in long leg braces but requires assistance for balance
8.	Stands in long leg braces but unable to walk even with assistance
9.	Is in a wheelchair
10.	Is confined to a bed

Table 2: Vignos scale