Hadassah O et al., / Vol. 06 / Issue 03 / 2018 / 67-72.

Research Article

Available Online at: www.ijphr.com
An African Edge Journal

International Journal of Pharmaceuticals and Health care Research

SJ Impact Factor (2015) – 5.546

ISSN: - 2306 – 6091

Duchenne muscular dystrophy (DMD) detail study

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ABSTRACT

Duchenne Muscular Dystrophy (DMD) is a highly severe type among all of inherited muscular dystrophies. It is considered to be the most common type of hereditary muscular disease without any bias in terms of race or ethnicity. The main cause of muscle weakness in this condition is the mutated gene dystrophin (muscular protein) which progressively leads to muscle degeneration. This disease initially starts up as muscle weakness and progressively ends up in a stage where the person loses the ability to carryout daily life activities and finally becomes wheelchair bound. The resulting complications of the condition are cardiac and orthopedic related. The onset of this condition is childhood. Death usually commences at the age of early 30's due to respiratory muscle weakness or cardiopathy which results in breathlessness or heart failure respectively. Therapy is usually cardiac oriented to reduce cardiac complications and physiotherapy is done to prevent orthopedic complications. There is no cure for this condition but treatment is given in order to reduce complications and provide muscular strength.

Keywords: Muscular Dystrophy, Dystrophin, X-linked recessive, Autosomal recessive, Eteplirsen.

INTRODUCTION

The word dystrophy is derived from the Greek language meaning dys- difficult ; troph- nourishment. Charles Bell was the first person who described muscular dystrophy. Duchenne Muscular Dystrophy is named after the scientist Dr.Duchenne de Boulogne who was from Paris. He was the first person to study muscular dystrophies during the mid-19th century .Muscular dystrophies include all types of inherited muscular disorders. There are about 20 muscular dystrophies. In general dystrophies result from gene faults. One or more genes responsible for muscle structure and functioning is defective mostly by mutation. They not only weaken muscles but progressively breakdown the muscles with time. Duchenne Muscular Dystrophy is statistically considered the second most common type of muscular dystrophy ,the first common being facioscapulohumeral dystrophy. One of the type of dystrophy closely relevant to Duchenne Muscular Dystrophy is Becker Muscular Dystrophy the only difference being the latter develops in later stages of life and exhibits milder symptoms. Duchenne Muscular Dystrophy develops at early childhood. The gene responsible for the disorder is present at the very birth of the child but there are no noticeable symptoms or muscle

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weakness. The muscle weakness is well exhibited at the age of 3 to 4 years. Initial symptoms are mild but progressively increase in the severity. According to a research done 2400 individuals in the UK itself suffer from the disorder. It is a X-linked recessive or autosomal recessive or autosomal dominant genetic disorder. It has an affect on boys majorly, exceptional cases are rare. In some cases the carrier women with the defective gene may end up showing some of the symptoms themselves but in very exceptional cases. The gene fault has a defecting affect on an important protein dystrophin of muscle fibers. This may otherwise occur by inheriting the defect for one of the parents. It is a non-curable disease. Medication is a prophylactic for further complications. Gene therapy for this disorder is in the early stage of study in humans.

AN OVERVIEW OF DIFFERENT TYPES OF MUSCULAR DYSTROPHIES

Becker Muscular Dystrophy

It is a variant of Duchenne muscular dystrophy but is a less severe condition. The dystrophin gene in this condition is either shortened or is partially functional. The rate of survival is more and extends into an old age. This condition is most likely to occur in males.

Congenital Muscular Dystrophy

This disorder onset is at birth causing muscle weakness and joint deformities which increases with age and the lifespan shortens. The affect may be either on the muscles alone or in cases may affect the brain and other organ systems. This condition occurs due to defect in proteins linked to dystrophin-glycoprotein complex. Some of the forms cause brain malformation referred to as lissencephaly and hydrocephaly.

Distal Muscular Dystrophy

The onset age group is between 20-60years. Weakness and wastage of muscles of hands, forearms and lower legs are a few symptoms. It is a slowly progressive condition but is not life threatening.

Emery Dreifuss Muscular Dystrophy

Occurs in childhood or early teenage. Signs clinically include muscle weakness and wasting. It starts at the distal -limb muscle and progresses to limb- girdle muscles. The possible complications included are cardiac defects commonly being arrhythmias.

Facioscapulohumeral Muscular Dystrophy

This condition initially affects the facial muscles which is progressively spread to the shoulders and upper arms leading to weakness. Symptoms are noticeable at late teenage. This occurs severely causing disability . In this condition spontaneously a number of mutations take place.

Limb Girdle Muscular Dystrophy

This affects both male and female. Upper arms and legs are equally weakened. An individual presents two copies of the defective genes one from each of the parents in autosomal recessive inheritance. Dominant forms are relatively low.

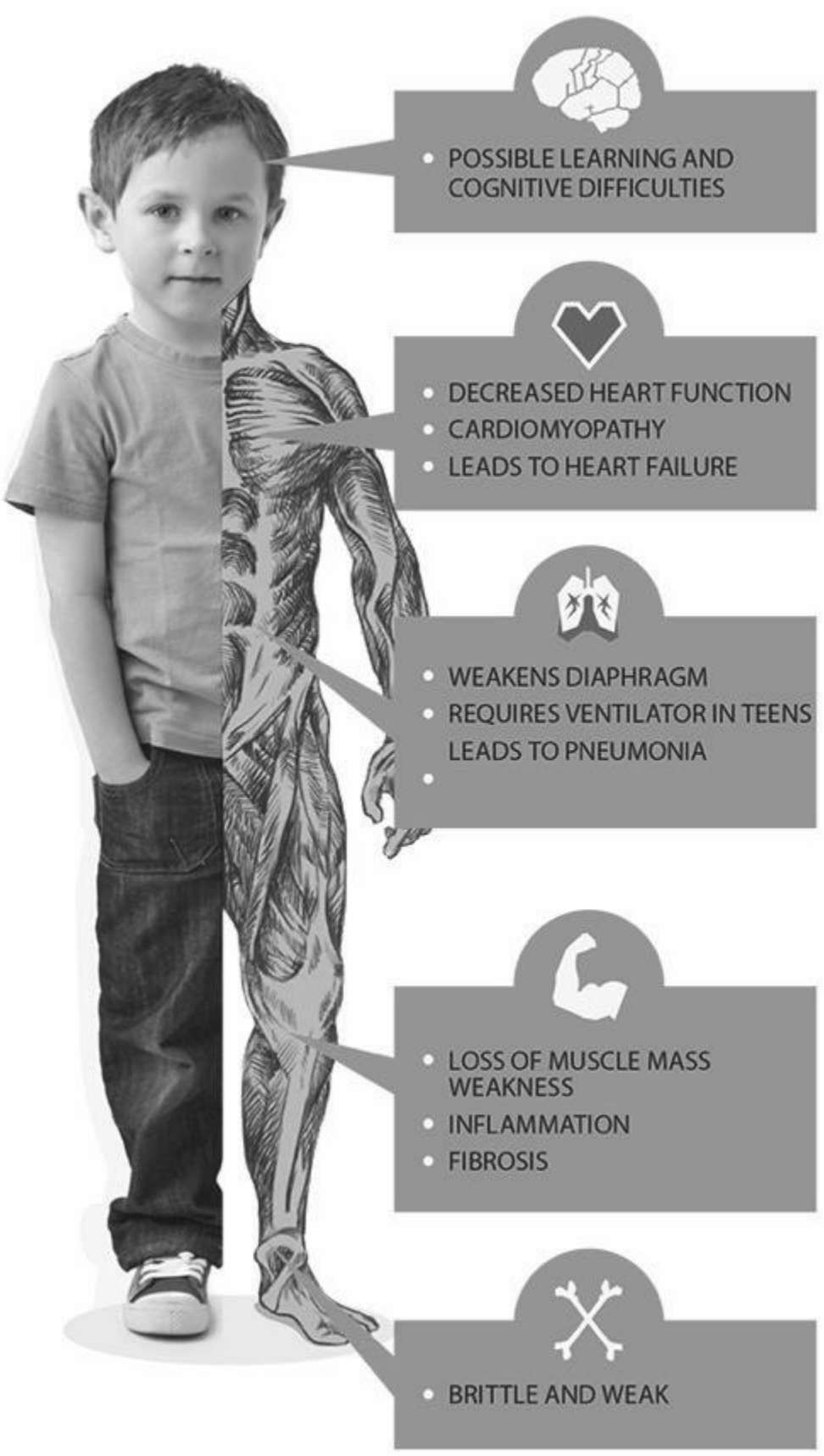
Normal lifestyle with support maybe possible but in cases may end up in death due to cardiopulmonary complications.

Myotonic Muscular Dystrophy

It is an autosomal dominant condition accompanied with delay in muscle relaxation. Myotonic Muscular Dystrophy is a common adult form caused from the repetition of a short DNA sequence. It is a rare condition and is also due to repeat in zinc finger protein gene.

Occulopharyngeal Muscular Dystrophy

Age of onset is between ages 40-70years. Affected areas are the eyelids, face, throat initially. Pelvic and shoulder muscle weakness occurs later. Short sequence repetition which is responsible for protein translation is the primary causative of the condition.


POSSIBLE LEARNING AND COGNITIVE DIFFICULTIES
DECREASED HEART FUNCTION
CARDIOMYOPATHY
LEADS TO HEART FAILURE
WEAKENS DIAPHRAGM
REQUIRES VENTILATOR IN TEENS
LEADS TO PNEUMONIA
LOSS OF MUSCLE MASS WEAKNESS
INFLAMMATION
FIBROSIS
BRITTLE AND WEAK

RISK FACTORS

As muscular dystrophies are due to gene defects either by mutation or inheritance of the defective gene the risk factors are related to the passing on of the defective gene and being inherited by the person.

a) Males are more prone to Duchenne Muscular Dystrophy as they exhibit only one X-chromosome unlike women, the Y-chromosome does not exhibit the dystrophin gene and thus the role of dystrophin is lost.
b) Females present an irregular gene which makes the woman a muscular dystrophy defective gene carrier. The risk of the offspring being affected is approximately considered to be 50%. If the offspring is a male the condition is highly sure to occur than in female offspring comparatively.
c) Family history of Duchenne muscular dystrophy is one of the possible risk factor for the occurrence of the condition. There may not be any proper stated reason for the passing down of the condition in the family. The family members are prone to carry forth the defective gene and may pass on for many generations before affecting a person.
d) Lifestyle risk factors include the condition of being underweight by body mass index, poor lung functioning and increased blood concentration of protein which results in cardiac damage.

DIAGNOSIS

For the purpose of diagnosis of any type of muscular dystrophy, the doctor collects information regarding the patient's family history. After the enquiry a few physical tests are performed. From the physical examination results a lot of understanding of the condition is obtained and also the pattern of weakness.

The types of physical tests performed are listed below:

Enzyme test:

Damaged muscles release enzymes, creatine kinase (CK) being the major enzyme. High CK levels in the blood though there is no occurrence of traumatic injury indicates a muscle disease might have occurred. In this test the blood of the individual is collected and checked for the presence of the CK enzyme. A high level of the enzyme assures the causative defect is due to muscle impairment and not the nerves. However the test does not determine the type of muscular disorder.

Electromyography

In this test an electromagnetic needle is injected directly into the muscle. The electrical activity whilst tightening and relaxing the muscle is recorded. The comparison of the electrical activity with the usual standards confirms the presence of any existing muscular dystrophy.

Genetic testing

In genetic testing the DNA sequence of any random cell is analyzed to see if there is any mutation in the dystrophin gene responsible for muscular dystrophy and if there is any such defect then found to where exactly it occurs. In case any male of the family is suffering from the condition the female relatives are tested to see if they are carriers of the disease.

Muscle biopsy

To carry out a muscle biopsy a fragment of the muscle is surgically removed through incision in any part of the body or with the aid of a hollow needle. Biopsy results confirm the type of muscular dystrophy and distinguish between inflammation or any other disorders. The amount of the dystrophin protein found in the biopsy confirms the type of muscular dystrophy for instance if no dystrophin is found it is confirmed to be Duchenne muscular dystrophy and if partial functional dystrophin is present the milder dystrophy that is Becker muscular dystrophy is confirmed.

Heart monitoring tests

Heart monitoring tests include electrocardiography and echocardiogram. These tests are done to analyze the heart functioning. It is done especially in individuals diagnosed with myotonic muscular dystrophy.

Lung monitoring tests

These tests are done in order to check the lung function as in few cases of muscular dystrophy the function of lung is affected.

Treatment

There is no treatment for Duchenne muscular dystrophy, how ever physical therapy, medications and surgeries are done in order to keep the person mobile for the possible amount of time and to avoid further complications. One of the aim is to provide muscle strength.

Medication

1. Eteplirsen is the first medicine specially used to treat Duchenne muscular dystrophy which was approved by the Food and Drug Administration. Usage is safe but the efficacy is not certain, it increases muscle strength.
2. Corticosteroids: Prednisolone is the opted corticosteroid in this condition. It's main action involves strength provision and also decreases the chances of other muscular dystrophies.
3. Angiotensin Converting Enzyme(ACE) inhibitors and Beta- Blockers usage slows down the process of deterioration of the cardiac muscles and reduces the risk of cardiac complications.

Physical Therapy

Physical therapies may include physiotherapy and also other assistive devices which improves the quality of life to some extent. The various possible physical therapies include the following

1. Stretching exercises: Muscular dystrophies result in stiffness and restricted mobility of joint muscles. Range of motion stretching keeps the joints flexible.
2. Physical exercises: Low scale exercises are opted such as walking which helps in retaining the muscle strength and its mobility. The exercises must be done under guidance or after a doctor's opinion as some exercises may be harmful and stressful on the muscles.
3. Braces: The use of braces keeps muscles and tendons stretched and flexible. They are used as a type of mobility aid and provides support to the weakened muscles.
4. Mobility aids: Canes, walkers and wheelchairs act as a support system for mobility.
5. Breathing assistance: In Duchenne muscular dystrophy the respiratory muscles are also weakened and the use of breathing assistance becomes necessary. Sleep apnea device helps in oxygen inhalation at night. In individuals with severe condition the use of ventilator for forced inhalation and exhalation becomes necessary.

Surgery

Duchenne muscular dystrophy results in spinal curvature and bent posture, in such conditions surgery is done to correct the posture as it may cause breathing difficulty.

Lifestyle and home remedies

Due to decreased mobility the person lacks in physical activity eventually resulting in weight gain and obesity. So a protein rich and fiber rich diet is necessary and the consumption of carbohydrates must be reduced.

CONCLUSION

Duchenne Muscular dystrophy is one of a few diseases that cannot be cured. Being a inherited disease it cannot be avoided otherwise. It ends up in impairment of mobility of the individual. The medication is focused on reducing the symptoms or to reduce the occurance of further complications.

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