Pediatrics and Neonatology (2017) xx, 1–8

Available online at www.sciencedirect.com

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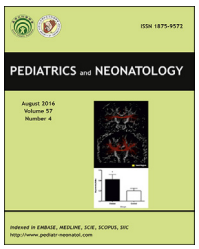

Original Article

The natural history of the patients with Duchenne muscular dystrophy in Taiwan: A medical center experience

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Received Oct 19, 2016; received in revised form Dec 24, 2016; accepted Feb 15, 2017
Available online ■ ■ ■

Key Words
corticosteroid;
Duchenne muscular dystrophy;
natural history;
Taiwan

Background: Duchenne muscular dystrophy (DMD) is the most common hereditary muscular dystrophy and caused by *DMD* gene mutation. In addition to progressive proximal muscle weakness, respiratory, orthopedic, and gastrointestinal complications are often observed in DMD. The natural history of patients with DMD in Taiwan has not been reported thus far.
Methods: Medical records of 39 patients who received a diagnosis of DMD between 1999 and 2016 at Kaohsiung Medical University Hospital were reviewed. The diagnosis of DMD was confirmed through muscle biopsy or *DMD* genetic analysis.
Results: The mean onset age and mean follow-up period were 2.75 years and 6.76 years, respectively. Seventeen patients (43.5%) had a family history of DMD. The mean full intelligence quotient of the patients was 71.08, and the mean age of walking ability loss was 9.7 years (25 patients). The mean onset age of respiratory insufficiency was 10.64 years with a decline rate of 5.18% per year (25 patients). The mean onset age of cardiomyopathy was 14.69 years (seven patients). The mean onset age of scoliosis was 13.29 years with a

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http://dx.doi.org/10.1016/j.pedneo.2017.02.004

Please cite this article in press as: Liang W-C, et al., The natural history of the patients with Duchenne muscular dystrophy in Taiwan: A medical center experience, Pediatrics and Neonatology (2017), http://dx.doi.org/10.1016/j.pedneo.2017.02.004

progression rate of 11.48° per year (14 patients).

Eleven (28.2%) and eight (20.5%) patients had deletions and duplications of *DMD*, respectively. Fourteen patients (35.9%) had point mutations or small deletions or insertions. Five patients received only multiplex ligation-dependent probe amplification (MLPA) analysis and exhibited neither deletion nor duplication. No mutation was identified in one patient through both MLPA and exon sequencing.

Conclusion: The clinical phenotypes and disease course in our cohort were consistent with that reported in previous studies. However, the proportion of point mutations or small deletions or insertions in our study was considerably higher than that in reports from other populations. Cardiac ejection fraction was found not a reliable biomarker for identifying cardiac problems, discovering a better parameter is necessary.

1. Introduction

Duchenne muscular dystrophy (DMD) is the most common hereditary muscular dystrophy. The prevalence of DMD is approximately 1 in 3800—6300 live male births.[1—3] DMD is caused by defects in the dystrophin gene (*DMD*), which is responsible for dystrophin production. Dystrophin is an integral part of the dystrophin—glycoprotein complex, which provides structural stability to the skeletal muscles by connecting the sarcolemma and the basal lamina to the inner myofibrillar network by associating with dystroglycan and cytoskeletal proteins. The absence of dystrophin destabilizes muscle membranes and makes them vulnerable to damage during muscle contraction. Different isoforms of dystrophin are derived from different promoters found in the brain, retina, and Purkinje cells. Mutations in these specific isoforms most likely cause extramuscular manifestations such as cognition, behavior, and learning problems.[4—6]

Typically, patients with DMD become symptomatic between 2 and 5 years of age, and their motor functions deteriorate significantly after the age of 5—7 years through progressive proximal muscle weakness. Patients with DMD usually lose the ability to walk by the age of 12 years. Marked progression of cardiac and respiratory dysfunction is observed during the teenage years. Orthopedic complications and gastrointestinal disturbances are also observed in these patients. In recent years, because of the advancements in cardiac and respiratory interventions, the patients' survival ages have extended to their thirties and forties.[7,8]

In the past decades, corticosteroid therapy has been reported to improve strength, pulmonary function, and timed motor function as well as reduce the need for scoliosis surgery and delay the onset and progression of cardiomyopathy in patients with DMD.[9—11] Additionally, comprehensive clinical care guidelines for DMD were proposed by an international, multidisciplinary group of experts and published in 2010, followed by several updated versions.[12,13] However, no cure for DMD is thus far available although many clinical trials of new therapeutic agents for DMD are underway with some promising results.[14,15]

This retrospective study analyzed the natural history of patients with DMD and evaluated the effect of steroid therapy, which has never been documented before in Taiwan.

2. Methods

2.1. Patients

We reviewed the medical records of patients who had received a diagnosis of DMD between 1999 and 2016 at Kaohsiung Medical University Hospital. The diagnosis of DMD was confirmed by either muscle biopsy or mutation analysis of *DMD* by using multiplex ligation-dependent probe amplification (MLPA) with or without direct sequencing.

2.2. Study design

Information on the patients' clinical manifestations, serial results of lung function tests (forced vital capacity, FVC), echocardiograms, X-rays of the spine, full intelligence quotient (FIQ) scores, family histories, and genotypes were collected and analyzed. This study was approved by the Institutional Review Board of Kaohsiung Medical University Hospital.

The patients with DMD were divided into two groups, corticosteroid users and nonusers for further analyses. The corticosteroid regimen used in our cohort was prednisolone 0.75 mg/kg on alternate days. Corticosteroid users were defined as patients who had received prednisolone continuously for more than 1 year. Nonusers were defined as patients who had never received corticosteroid treatment or had received the treatment for less than 1 year. The duration of being ambulant, decline in the rate of FVC and left ventricle ejection fraction (LVEF), and rate of scoliosis progress were compared between the two groups. The percentage of predicted FVC calculated from healthy individuals was used for analysis. A patient was considered to exhibit respiratory insufficiency if the FVC was lower than 80% of the predicted value. Data obtained from patients younger than 6 years were excluded because of poor

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