Serum Level of Brain Natriuretic Peptide (BNP) in Pediatric Patients with Muscular Dystrophy

Thesis

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(قَالُوا سُبْحَانَكَ لَا عِلْمَ لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنتَ الْعَلِيمُ الْحَكِيمُ)

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Yasmin Mohamed Ahmed Ismail

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Abstract

Background: Duchenne muscular dystrophy (DMD) patients used to die mainly from pulmonary problems. Echocardiography remains the standard diagnostic modality for cardiomyopathy in DMD patients, but is hampered by scoliosis in adult DMD patients. We investigated the usefulness of the plasma concentration of brain natriuretic peptide (BNP) for evaluating cardiac affection in patients with DMD.

Methods: The plasma BNP concentration was measured by immunoassay in 15patients with DMD and in 15 healthy children. Cardiac function was evaluated by echocardiography which classified left ventricular function as preserved or depressed, and BNP. The function of skeletal muscle was evaluated by the disability of lower limb function, CPK.

Results: The plasma concentration of BNP was increased in patients with DMD (95.700±58.901pg/ml, mean +/- SD) compared with that in normal children (16.007±7.135pg/ml). Four of the DMD patients had symptoms of heart failure, with markedly increased plasma BNP concentrations. The other DMD patients with increased plasma BNP concentrations showed abnormal cardiac function but no symptoms of heart failure. In addition, in patients with DMD, the plasma BNP concentration showed significant positive correlations with duration of cardiac affection, and negative correlations with CPK and LVEF. There was no significant correlation with duration of muscular dystrophy disease.

Conclusion: The combination of echocardiography and BNP achieves good results in the evaluation of left ventricular function. We advise to add BNP to echocardiography in the routine cardiac assessment of DMD patients.

List of Contents

List of Figures

List of Figures (Cont.)

List of Tables

List of Tables (Cont.)

List of Abbreviations

Abbrev.	
AD	Autosomal Dominant
ADP	Adenosine Diphosphate
AR	Autosomal Recessive
BMD	Becker muscular dystrophy
BNP	Brain Natriuretic Peptide
CMD	Congenital Muscular Dystrophy
CT.....	Computed Tomography
CTG	Cardio Toco Graph
CPK	Creatine Phosphokinase
DAG.....	Dystrophgin Associated Glycoprotein
DCM	Dilated cardiomyopathy
DMD	Duchenne Muscular Dystrophy
ECG.....	Electrocardiogram
EDMD.....	Emery-Dreifuss Muscular Dystrophy
EMG	Electromyograph
FCMD	Fukuyama Congenital Muscular Dystrophy
FSHD.....	Fascioscapulohumeral Muscular Dystrophy
LGMD	Limb-Girdle Muscular Dystrophy
MD.....	Muscular Dystrophy
MMD.....	Myotonic Muscular dystrophy tonic Muscular Dystrophy

List of Abbreviations (Cont.)

Abbrev.	
MUAPs	Motor Unit Action potentials
MUGA	Multigated cardiac radionuclide ventriculography
OPMD	Occulopharyngeal uscular Dystrophy
PCR	Polymerase Chain Reaction
RESNA	Rehabilitation and assistive Technology Engineering Society of North America
ROC	Receiver operating characteristic curve
WAIS	Wechsler Adult Intelligence Scale
XR	X-linked Recessive

Introduction

The muscular dystrophies are a group of muscle disorders characterized by progressive muscle wasting and weakness. Age of onset is variable, as are the distribution and severity of the diseases. Muscular dystrophies are caused by gene abnormalities, which code for a variety of proteins involved in different functions ***(Seidman and Seidman, 2001).***

Duchenne muscular dystrophy (DMD) is a common genetic disease which is an X - linked recessive disorder caused by a mutation on the dystrophin gene, located on chromosome Xp 21. The gene normally codes for a protein, dystrophin, which links cytoplasmic actin to the dystrophin - glycoprotein complex at the cell membrane. Dystrophin loss leads to muscle cell structural instability ***(Allikian et al., 2003).***

The dystrophin gene has been shown to be the cause of X-linked dilated cardiomyopathy and some cases of sporadic dilated cardiomyopathy. The time course for the development of cardiomyopathy has not been well characterized; however, clinical studies demonstrate that the disease process in the heart is underway long before symptoms appear ***(Giglio et al., 2003).***

Signs of cardiac dysfunction may be vague and nonspecific, such as fatigue, weight loss, vomiting, or sleep disturbance. Currently at many medical centers, affected individuals do not come to the attention of the cardiac specialist until late in the disease process, when the clinical manifestations of cardiac dysfunction become evident. This reactive, rather than proactive, approach must change if progress is to be made in the treatment of dilated cardiomyopathy in this patient population ***(Bourke et al., 2003).***

Cardiac involvement is common and increases with age in pediatric patients with muscular dystrophy. A range of 10 – 15 % of patients will die from the consequences of left ventricular failure.Cardiac rhythm abnormalities are frequent and play a significant role in morbidity and mortality in muscular dystrophy. The most common electrocardiographic abnormality is sinus tachycardia, with prevalence of approximately 90% ***(Finsterer and Stollberger, 2005).***

Aim of the Work

The aim of the present study is to evaluate Plasma concentration of brain natriuretic peptide (BNP) as a prognostic marker for cardiac affection in pediatric patients with muscular dystrophy.

Muscular Dystrophy

Definition

Muscular dystrophy (MD) is a group of muscles diseases that weaken the musculoskeletal system and hamper locomotion. Muscular dystrophies are characterized by progressive skeletal muscles weakness, defect in muscle proteins, and the death of muscle cells and tissue ***(Emery,2002)***.

Historical View

Muscular dystrophy (MD) is a collective group of inherited noninflammatory but progressive muscle disorders without a central or peripheral nerve abnormality. The disease affects the muscles with definite fibre degeneration but without evidence of morphologic aberrations. The first historical account of muscular dystrophy was reported by Conte and Gioja in 1836. They described 2 brothers with progressive weakness starting at age 10 years. These boys later developed generalized weakness and hypertrophy of multiple muscle groups, which are now known to be characteristic of the milder Becker MD. At the time, however, many thought that Conte and Gioja described tuberculosis; thus, they did not achieve recognition for their discovery ***(Conte and Gioja,1836)***.