The Egyptian Journal of Medical Human Genetics (2014) **15**, 79–85

Ain Shams University

The Egyptian Journal of Medical Human Genetics

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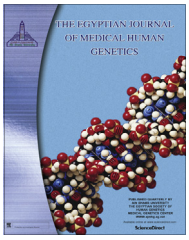

ORIGINAL ARTICLE

Assessment of respiratory involvement in children with mucoplysaccharidosis using pulmonary function tests

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Received 12 August 2013; accepted 30 September 2013
Available online 20 October 2013

KEYWORDS

Mucopolysaccharidosis;
Pulmonary function tests;
Impulse oscillometry;
Whole body plethysmography

Abstract *Background:* Mucopolysaccharidosis (MPS) are classified into seven clinical types based on eleven known lysosomal enzyme deficiencies of glycosaminoglycan (GAG) metabolism. Respiratory involvement seen in most MPS types includes recurrent respiratory infections, upper and lower airway obstruction, tracheomalacia, restrictive lung disease, and sleep disturbances.

Aim of the study: To delineate the pattern of respiratory compromise and pulmonary function abnormalities in MPS patients.

Methods: This is a cross section observational study conducted on 30 patients recruited from the Neurometabolic Clinic, Children's Hospital, Cairo University over a period of 18 months. All patients were screened first by the quantitative determination of GAGs in urine, and diagnosis was confirmed by unidimensional electrophoresis for GAGs in urine and/or specific enzymatic assay in blood leucocytes. Infant pulmonary functions (IPFT) were done in twenty-two patients (<3 years of age), while 8 cases performed impulse oscillometry (IOS) test (3–6 years of age).

Results: Ages at diagnosis ranged from 1 to 9 years with a median of 2.3 years. Male to female ratio was 4:1. Consanguinity was observed in 53.3% whereas similar family condition was present in 40% of cases. Lumbar kyphosis was detected in 60% of cases, while scoliosis was detected in 46.7%. Results of pulmonary functions were mainly obstructive in 20 (66.6%) cases; however, combined obstructive and restrictive were detected in only 6 (20%) of cases. Data showed no association

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Peer review under responsibility of Ain Shams University.

ELSEVIER Production and hosting by Elsevier

http://dx.doi.org/10.1016/j.ejmhg.2013.09.004

between the presence of scoliosis or the presence of organomegaly and the pattern of pulmonary function abnormalities.

Conclusions: Evaluation and follow up of patients with MPS using pulmonary function tests are essential to detect early involvement of respiratory system and hence start treatment for respiratory complications early in the course of the disease.

1. Introduction

The mucopolysaccharidosis (MPS) are lysosomal storage disorders caused by the deficiency of enzymes required for the stepwise breakdown of glycosaminoglycans (GAGs), also known as mucopolysaccharides. These conditions are differentiated by their clinical features and age of presentation. MPS are rare conditions; with an estimated total incidence of approximately 1/20,000 live births [1].

Respiratory complications affect patients with all types of MPS and contribute to death and disability as their disease progresses. Respiratory abnormalities result from airway obstruction, excessive secretions, skeletal restriction and frequent infections. Progressive deposition of GAGs in the soft tissue of the throat and trachea is thought to be responsible for the airway obstruction and dysfunction. These problems can lead to progressive respiratory insufficiency, severe sleep apnea, and sudden death from central apnea [2].

Few studies were published about respiratory functional assessment in MPS patients. The availability of new measurement systems specifically tailored to pediatric patients now allows clinicians to diagnose and follow up deterioration of lung function, which was previously challenging in this population [3].

2. Aim of the present study

The aim of the study is to assess the pattern of respiratory compromise and pulmonary function abnormalities in MPS patients.

3. Subjects and methods

3.1. Study design and sampling

This cross section observational study was conducted on 30 cases diagnosed as MPS and was followed up in the Neurometabolic Clinic at Children's Hospital, Cairo University over a period of 18 months (from March 2011 till September 2012). This work was carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki) and was approved by the Faculty of Medicine, Cairo University Ethics Committee. Informed consents were received from the families of all participants in Arabic before being enrolled in this study.

3.2. Methods

MPS patients were screened first by the quantitative determination of GAGs in urine, and diagnosis was confirmed by unidimensional electrophoresis for GAGs in urine and/or specific enzymatic assay in blood leucocytes. Quantitative GAG analysis was performed using the dimethyl-methylene blue (DMMB) method [4]. Cellulose acetate was used to differentiate and identify different types of sulfated glycans extracted from urine in electrophoresis using Barium acetate solution (12%) as a buffer medium and DMMB as a colorant [5]. The resulting bands were compared with the bands of GAG standard mix solution in every run. Specific enzymatic activities using fluorescent substrates α-L-iduronidase for Hurler-Scheie [6], iduronate-sulfatase for Hunter [7], heparin-sulfamidase for Sanfilippo type A [8] and galactose 6-sulfate sulfatase for Morquio type A [9] were performed in the homogenates of patients' leucocytes and referred to the total protein content of the sample.

All selected MPS patients were subjected to comprehensive clinical evaluation including general, respiratory, cardiac and neurological clinical history and examinations. Magnetic Resonance Imaging (MRI brain), electrocardiography (ECHO) as well as ear nose and throat (ENT) examinations were done to all recruited cases.

Pulmonary functions using infant lung functions (IPFT) for infants < 3 years old, while impulse oscillometry (IOS) was used for preschool children aged 3–6 years. Infant pulmonary functions tests were performed using Master screen Babybody (V.4.53 Erich Jaeger GmbH, Wurzburg, Germany) [10]. Routine safety measures in pulmonary function test laboratory were taken including full resuscitation equipment, two trained personnel during testing, continuous monitoring using pulse oximetry, use of transparent face mask and adherence to a specific protocol for sedation. Patients with any contraindication to perform pulmonary functions as severe upper respiratory obstruction were excluded from the study. Patients with history of upper respiratory tract infections were deferred for 3 weeks following attack. Length and weight were measured on each occasion together with proper posturing to avoid flexion or rotation of the neck. Fasting was not indicated. Reference values for the supine position were available [11,12].

The following IPFT parameters were measured:

(1). Tidal breathing parameters were measured by a pneumotachograph attached to a face mask, tidal breathing was recorded in epochs of 30 s. Each epoch contains at least 20 breaths. The mean of five trials was reported [13].
(2). The single occlusion technique was used for measuring passive respiratory mechanics in this study. The equipment used for the occlusion techniques included a shutter, flowmeter, and transducers [14]. The length of the occlusion was set at 400 ms. The occlusion was automatically stopped once an adequate plateau had been reached. The occlusion was also automatically stopped if the infant inspires against the closed valve, and the maximum length of the occlusion was set at 1000 ms.