Diagnosis and treatment of individuals with MPS II Hunter disease in the United Kingdom

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Introduction

1Hunter disease (MPS II) is a rare, X-linked disease which is caused by a deficiency of iduronate-2-sulfatase, leading to a progressive accumulation of glycosaminoglycans in cells, tissues and organs.1,2

2Individuals with MPS II experience a range of clinical manifestations, including airway obstruction, skeletal deformities and cardiac disease. Individuals with central nervous system (CNS) involvement, experience cognitive impairment and neurological decline.1,2

3MPS II signs and symptoms typically manifest between 18 months and 4 years in individuals with the attenuated phenotype; this is further delayed by around 2 years in the severe phenotype.3

4The first diagnostic approach, and the one that patients and their carer’s generally remember, is urinary DAG assessment.

5Urinary analysis can indicate the presence of an MPS disorder, but a definitive MPS II diagnosis is via blood enzyme analysis; the best practice followed in the UK is that a positive urinary DAG result is followed by a blood test or genetic testing.

6Prenatal diagnosis is available for foetuses at risk of MPS II.4

7Whilst enzyme replacement therapy (ERT) has been shown to improve the signs, symptoms and wellbeing of individuals with MPS II, data on haematopoietic stem cell transplantation (HSCT) are rare.4

8The aim of this project was to understand how and when MPS II is diagnosed and treated in the UK and to determine the prevalence of CNS involvement and concomitant diagnoses.

Methods

1Seventy-one individuals with MPS II resident in the UK were identified by the MPS Society and invited to take part in the survey via telephone interview.

2A specifically designed questionnaire was used to assess the individual’s diagnosis and treatment as well as their educational attainment and need for support from primary through to further education.

3Interviews took place in December 2015 and January 2016.

4Results for the diagnosis and treatment section of the survey are presented here.

5Results for the educational attainment and support from primary through to further education are presented in Poster 164.

Results

Diagnosis

1Forty-one individuals agreed to take part in the study (58%), ranging in age from 1 to 36 years (mean 12.5 years).

2Age at diagnosis of MPS II ranged from 6 days to 7 years (mean 2.5 years).

3Diagnosis was earlier in the younger individuals (under 8 years), with a mean of 18 years (range 6 days to 3 years), compared to a mean of 2.5 years (range 6 months to 7 years) in those aged 8 years and over.

4Fifty-five percent of individuals had seen other physicians or specialists before their MPS II diagnosis (Figure 1).

5There was one report genetic testing (2%) which had taken place outside of the UK. This took place in the absence of blood and/or urine enzyme analysis.

6One individual reported hair/instol analysis as part of their MPS II diagnosis; this was carried out in addition to blood and urine enzyme analyses.

7Concomitant diagnoses were made in 7 individuals (17%). Attention deficit hyperactivity disorder and autistic spectrum disorder were the most prevalent concomitant diagnoses (Figure 3), all concomitant diagnoses were made after the diagnosis of MPS II.

8Of the 41 individuals surveyed, 54% (n=22) reported CNS involvement, 37% (n=15) reported no CNS involvement; four individuals (10%) did not know whether there was CNS involvement or not.

9A review of all responders data indicated all but 3 had some level of CNS involvement; 49% (n=20) had severe progressive CNS involvement.

9Treatment

1Ten ninety-three (53%) of individuals were being or had been treated with ERT, including individuals receiving or who had received intravenous ERT and those participating in a clinical trial for intrathecal ERT.

2Overall, the mean age at start of ERT was 5.9 years (range 8 weeks to 27 years).

3Children born since the reimbursement of ERT (2007 in England, Scotland and Northern Ireland) started ERT earlier than the overall population, with a mean age of 2.4 years (range 8 weeks to 4 years).

4Four individuals (10%) received a HSCT; 3 individuals were under 1 year (8 weeks, 4 months and 10 months); the other aged 2 years and 3 months, at the time of the transplant.

5Half of the individuals who received a HSCT, also received ERT at some point in their treatment.

6HSCT consisted of bone marrow (n=2) and cord blood (n=2). No individuals received mobilised peripheral blood stem cells.

7One individual (2%) had not received any form of treatment for MPS II.

Conclusions

1MPS II is being diagnosed at an earlier age, but in the UK it can still take up to 3 years to obtain a definitive diagnosis. This is in line with other published findings.

2Individuals are often referred to one or more specialists before an MPS II diagnosis is reached; with specialist involvement dependent upon presenting features.

3Most individuals are being treated with ERT and following the reimbursement of ERT in 2007, normally start treatment before the age of 3.

4In agreement with the literature, only a small proportion of individuals in the UK receive a transplant as part of their treatment for MPS II.4

References


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The data supporting this poster were gathered via a questionnaire filled in by patients or their carer’s. The accuracy of the data in these patient reported outcomes cannot be confirmed without consulting the respective patient medical records.