Journal of Neuromuscular Diseases 1 (2015) S40
DOI 10.3233/JND-159036
IOS Press

Poster Abstract: Diagnostic

Establishment of a Screening Test for Rapid and Early Diagnosis of Pompe Disease using Tandem Mass Spectrometry (Lc-Ms/Ms): Israel Experience

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BACKGROUND

Pompe disease is an autosomal recessive disorder, caused by deficiency of acid alpha-glucosidase (GAA), which results in lysosomal accumulation of glycogen in multiple organs, with prominent involvement of heart and skeletal muscle. Early diagnosis is highly important, since prompt initiation of enzyme replacement therapy may improve morbidity and mortality.

AIMS

1. To establish the utility of a tandem mass spectrometry (LC-MS/MS) method to measure GAA activity for screening Pompe disease among the population in Israel.
2. To study 5,000 dried blood spots (DBS) from infants born in Israel to generate GAA reference ranges in the Israeli population.
3. To establish a first-line rapid test for diagnosis of Pompe disease in Israel.

METHODS

A 3-mm DBS punch was incubated in a single assay buffer with substrate and internal standard. The samples were processed by a liquid–liquid extraction by using ethyl acetate, dried and resuspended in solvent for injection into the tandem mass spectrometer. Products and internal standards were monitored by multiple reaction monitoring.

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RESULTS

Assay for GAA enzyme was successfully achieved with acceptable statistics.

The entire procedure fits into a 60-h cycle, including data analysis. To ensure the quality management system of our testing performance for each run, appropriate blanks, a series of calibration and at three levels (low, medium, and high) of control sample received from the Centers for Disease Control and Prevention (CDC), were included. We established our own references which were similar to the CDC references. Data from 5,030 anonymous newborn DBS samples showed an approximate bell-shaped distribution of enzymatic activities. Mean values ± two standard deviations of 12.46 (±5.37), μmol/h/L blood were calculated. Abnormal GAA activity (less than 2 μmol/h/L blood) was established and was similar to the published data. Since the introduction of this technique, we have studied 76 DBS samples from patients presenting with muscle weakness, respiratory insufficiency, and/or cardiomyopathy that were referred to our metabolic laboratory. Eight new infantile Pompe patients were diagnosed with the mean activity of 0.79 (±0.57) μmol/ h/L blood. The underlying mutations were confirmed in all patients.

CONCLUSION

In our experience, the LC-MS/MS GAA activity assay provides a rapid and reliable first-tier test for early diagnosis of patients suspected of having Pompe disease for timely treatment.

ISSN 2214-3599/15/$27.50