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Poster Abstract: Diagnostic

Screening for Pompe Disease in Specific At-Risk Populations with Sleep-Disordered Breathing

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BACKGROUND

Pompe disease (PD) is a rare autosomal recessive muscular disease, caused by deficiency of the acid α-glucosidase (GAA) enzyme. Nocturnal hypoventilation due to diaphragmatic weakness or rapid eye movement (REM)-predominant sleep-disordered breathing (SDB) may be presenting features. Diagnosis of PD previously required detection of reduced GAA activity in tissue, but a convenient dried-blood spot (DBS) test has recently been developed. Recombinant human GAA enzyme replacement therapy is now available. Our aim was to determine the prevalence of PD in two specific populations: 1) Patients requiring home ventilatory assistance for chronic respiratory failure of no clear etiology, and 2) patients with REM-predominant SDB.

METHODS

Records were reviewed from the McGill Home Ventilation program (Group 1) and from the sleep laboratory (Group 2). Group 1 individuals were included if there was lack of a specific and unequivocal diagnosis accounting for their respiratory failure, and Group 2 individuals if they had REM-predominant obstructive sleep apnea or hypoxemia. Subjects underwent DBS testing and serum creatine kinase (CK) measurement. Abnormal DBS results were further validated by (partial) gene sequencing.

RESULTS

Of the 8258 screened records, 660 patients (73 from Group 1; 587 from Group 2) were eligible. Of these, 252 subjects participated to date (67 from Group 1; 185 from Group 2). Initial DBS was abnormal in six subjects (one from Group 1 and five from Group 2), all of whom had normal CK levels. Repeat testing confirmed abnormal GAA activity in one subject, who was found to have a single mutation (C to T variant in exon 17); another subject with an initially low DBS value was found to have a single mutation (deletion in exon 18). None of the patients had clinical signs of significant muscle weakness.

CONCLUSIONS

In this exploratory study of selected at-risk patients with SDB, DBS screening is feasible. Although heterozygous carriers were identified, no clinical cases of PD were found. Occasional false-positive DBS values do occur, and in all cases results must be interpreted in light of the clinical context.

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