

Poster Abstract: Diagnostic

Breathing Pattern and Central Ventilatory Drive in Late-Onset Pompe Disease

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INTRODUCTION

Pompe disease is an autosomal recessive disorder characterized by acid alpha-glucosidase (GAA) deficiency that results in intralysosomal glycogen accumulation affecting skeletal muscles with more specific impairment of proximal limb, trunk, and respiratory muscles. Pulmonary symptoms may represent one of the initial manifestations of late-onset Pompe disease (LOPD) in patients, even those still ambulating, and may include exertional dyspnea, sleep disordered breathing, impaired cough, and chronic respiratory insufficiency. LOPD respiratory disturbances have commonly been attributed to muscle deficiency, mostly diaphragmatic. Since glycogen accumulation has been documented in the peripheral nerves (i.e. the phrenic nerve) and the central nervous system (brainstem and spinal motoneurons), either in patients or in animal models, a potential neural respiratory control dysfunction has also been postulated. The aim of this study was to determine the breathing pattern and central ventilatory drive in patients with LOPD to better understand the pathophysiology of their respiratory impairment.

MATERIAL AND METHODS

Twenty patients with LOPD (11 males and 9 females) aged 14–82 years (48±20) were studied and compared with a control group of 20 age- and sex-matched healthy individuals and with 16 patients with myotonic dystrophy 1 (DM1), aged 11–62 years

(46±13). Investigations were started at the same time in the morning under basal conditions for all patients. Pulmonary function tests (forced vital capacity [FVC] in sitting and supine positions, maximal inspiratory pressure and maximal respiratory pressure) and respiratory breathing pattern (inspiratory time [Ti], total duration of respiratory cycle [TTot], duty cycle [Ti/TTot], Vt/Ti, RF, respiratory shallow breathing index [RSBI]) with inspiratory occlusion pressure in the mouth in the first 0.1 second (P0.1) were performed.

RESULTS

Among the ventilatory pattern parameters, LOPD patients showed a consistent decrease in P0.1, Ti, Ttot and Vti ($P<0.05$) when compared with controls, whereas respiratory rate (RR), and respiratory shallow breathing index (RSBI) were significantly increased ($P<0.001$). Compared with DM1 patients, mouth occlusion pressure after 0.1 second after onset of inspiratory effort [P0.1], Ti, effective impedance [P0.1/(Vt/Ti)], Ti/Ttot, mean inspiratory flow [Vti/Ti], RR, RSBI, Δ FVC were significantly reduced ($P<0.05$). No correlations were found between breathing pattern and pulmonary function parameters.

CONCLUSIONS

These findings show that LOPD patients had a breathing pattern and respiratory control different from either healthy subjects or patients with a prominent myopathic involvement (DM1), suggesting an impaired neural control of breathing that can contribute to respiratory failure in LOPD patients. This might be due to glycogen accumulation in peripheral and central nervous systems.

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