Myopathy and Dysphagia in Adults with Cystinosis

Stacey Sullivan, MS, CCC-SLP and Natalie Grant, BA
Massachusetts General Hospital

Distal myopathy and dysphagia are common in patients with nephropathic cystinosis; however, little is known about the pathophysiology of these manifestations. In order to implement clinical trials for the treatment of myopathy, it is crucial to have a better understanding of the characteristics and evolution of these symptoms. In addition, there is a need for outcome measures that can detect subtle abnormalities and longitudinal changes in disease status.

In a previous clinical trial readiness study, we sought to further characterize dysphagia and distal myopathy and evaluate longitudinal changes over a one-year period. We administered video swallow studies, respiratory function measurements, tests of muscle strength, and questionnaires to assess for presence of myopathy and dysphagia symptoms. We found that 70% of patients experienced symptoms of distal weakness and 85% of patients experienced signs of distal weakness. Whereas 60% of patients reported symptoms of dysphagia, only 30% of patients showed evidence of dysphagia on swallow studies using the Penetration-Aspiration Scale (PAS). There was a significant decline in leg strength after the one-year period, but no changes were found in swallowing or breathing outcomes. Only 2 patients had worsening PAS scores, indicating that currently used rating scales were not sensitive enough to detect changes over time.

We are currently conducting Phase III of our study, which has three objectives: 1) to determine the degree of myopathy in the most affected distal upper and lower extremity muscles using electrodiagnostic techniques; 2) to further characterize dysphagia using more sensitive swallowing biomarkers (MBSImP) and determine the most affected swallowing muscles; and 3) to determine the pathological features of skeletal muscle cells in patients with cystinosis and determine the feasibility of potential future regenerative treatment. Our third objective is being done in collaboration with the Rubin lab at Harvard Stem Cell Institute. We have enrolled 4 patients in the study thus far and 2 muscle biopsies have been collected for analysis.

In parallel with Phase III of our study, we conducted a retrospective analysis of all 59 swallow studies performed in Phase I and II of the study. We sought to characterize oral, lingual, and pharyngeal swallowing physiology using MBSImP in order to better understand which components of swallow function are impaired. Our analysis highlighted impairments in swallowing across multiple domains in both the oral and pharyngeal phases of swallowing. In particular, >50% of patients demonstrated difficulties of tongue control during bolus hold, reduced lingual motion, presence of oral residue, reduced laryngeal elevation, reduced tongue base retraction, and presence of pharyngeal residue, deficits that were not captured using PAS. Both MBSImP oral and pharyngeal scores correlated with patient-reported swallowing difficulty, indicating that MBSImP has the ability to capture more subtle changes relevant to patient symptoms.