REiNS functional working group

Winter 2017 Meeting
December 4, 2017
Goal

• To identify standardized functional measures appropriate for use as endpoints in NF clinical trials
• Functional measure outcomes
  – Outcomes that focus on a patient’s ability to perform specified activities that are a meaningful (to the patient), part of typical (e.g., daily) life
• Our group reviews measures for types of physical functioning that can be affected by NF
  – hearing, facial function, pulmonary function (breathing), walking and sleep
For hearing endpoints, the functional group endorsed the use of maximum word recognition score as a primary endpoint, with the 95% critical difference as primary hearing outcomes.

The group recommended use of the scaled measurement of improvement in lip excursion (SMILE) system for studies of facial function.
• For patients with airway PNs, polysomnography, impulse oscillometry, and spirometry should be performed to identify abnormal function that will be targeted

• The functional group endorsed the use of the AHI as the primary sleep endpoint, and pulmonary resistance at 10 Hz (R10) or forced expiratory volume in 1 or 0.75 seconds (FEV1 or FEV0.75) as primary pulmonary endpoints
Overview of ongoing projects

• Outcome measures for assessing muscle strength
  – Srivandana Akshintala, David Stevenson

• Dysphagia outcome measures
  – Heather Thompson, Ann Blanton
Assessing muscle strength

• A pilot study of using hand held dynamometry for muscle strength testing in children and adults with NF
  – Primary objective: To assess the reliability of measuring muscle strength using HHD

• Muscle weakness has been described in NF
  – primary myopathy, central nervous system dysfunction, abnormalities of peripheral nerves, spinal tumors

• Clinical trials targeting PNs in children with NF1 have anecdotally shown to decrease functional impairments including muscle weakness

• Functional outcome measures are therefore needed to assess clinical benefit, in particular, muscle strength
Methods for strength testing

- Manual Muscle Testing
- Isokinetic dynamometers
- Hand held dynamometry
- Handgrip strength

HHD
- Has been validated against isokinetic dynamometers
- Reliability studied in many patient populations with performance varying based on patient population and muscle group being tested
- Has been used as an efficacy measure in clinical trials for amyotrophic lateral sclerosis

Douma et al 2014
Study design

• Key eligibility
  – Patients ≥ 5 years with clinically confirmed NF1 or NF2 or a known NF mutation
  – At least 1 muscle group that is weak per MMT (<5/5 strength) out of a list of pre-selected potential muscle groups

• Study design
  – Evaluate muscle strength in 20 patients using HHD
  – Assess strength in 2 muscle groups 3 times each
  – Obtain clinical data such as age, sex, weight, height, handedness, muscle strength by MRC scale, and h/o NF manifestations
  – Assess reliability of strength measurement using ICC
Dysphagia outcome measures

- Dysphagia refers to disorders related to swallowing
  - Occurs in individuals with Neurofibromatosis
- Extensive literature search performed (Spring 2017)
- Outcome measures considered
  - Bedside swallowing screen (3oz water test)
  - Endoscopic Evaluation of Swallowing (FEES)
  - Videofluoroscopic Evaluation of Swallowing (VFSS)
- Recommendations
  - Three ounces of water test + pulse oximetry for screening
  - Videofluoroscopic Study for further evaluation following a failed screening
    - Modified Barium Swallow Tool (MBSImp, Martin-Harris et al., 2008)
    - Penetration-aspiration scale (Coyle, 2017)
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REiNS
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