Developing the SMA REACH UK database: A combined effort to improve standards of care and translational research in Spinal Muscular Atrophy

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Background:
Exciting developments in the field of Spinal Muscular Atrophy mean there are potential therapeutic treatments on the horizon for this debilitating disease. Such advancements require robust validated outcome measures for clinical trials and agreed standards of care. A number of functional scales have been used in the last few years for SMA; while they capture important aspects of SMA function, each has shortcomings evident both clinically and when tested with modern psychometric techniques.

A new study SMA REACH UK (SMA Research And Clinical Hub) aims to frame a national UK network, with robust links to other international networks, to establish and implement optimal functional assessment tools and standards of care for patients with SMA, thereby facilitating translational research.

SMA REACH UK has been working with international partners, the Italian SMA Network and the Pediatric Neuromuscular Clinical Research Network (PNCR) for SMA in the US, on a collaborative initiative to make the necessary improvements to functional scales to ensure they are robust for both clinical and research purposes.

This poster reports on the work completed to date on the UK experience of the development of novel outcome measures and their clinical trial readiness, with particular reference to the Revised Hammersmith for SMA (Draft).

Functional Outcome Measures in SMA & Development of Novel/Exploratory Scales “Plan B”:
Since it’s inception SMA REACH UK has held two workshops in London (December 2013 & May 2014) with international expert Physicians and Physiotherapists in the field of SMA from the UK, Italy and US. The purpose of these workshops was to discuss the status of current outcome measures in light of the paper by Cano et al (2013)1 and the experience of SMA Europe. This has resulted in an international collaborative effort to improve functional measures to ensure the motor abilities of people with SMA are captured using robust scales tested with both traditional and modern psychometric techniques.

These workshops centred on clinically reported functional scales designed for use in SMA types 2 & 3 as detailed in Figure 1. Each scale was discussed regarding clinical trial readiness, lessons learnt from SMA Europe, available Rasch analysis, clinical meaningfulness, and sensitivity to change.

This resulted in the creation of novel/exploratory measures based on the Hammersmith Functional Motor Scale Expanded2 and Upper Limb module for SMA.

UK SMA Network:
The SMAntNet clinical database for SMA was established in 2006 as a national multi-centre clinical network for Spinal Muscular Atrophy in the UK. The SMAntNet database currently has 193 registered patients with SMA types 2 & 3 registered across 11 sites in the UK. This database holds anonymised clinical information from routine medical and physiotherapy assessments and is supported by the Muscular Dystrophy Campaign.

SMA REACH UK will expand upon the foundational work started by SMAntNet, to ensure the UK is clinical trial ready. This project is being led by the Dubowitz Neuromuscular Centre at University College London in collaboration with the MRC Neuromuscular Centre in London and Newcastle, and Newcastle University. Recruitment to SMA REACH UK commenced in February 2014, current sites are London and Newcastle with the aim to expand nationally. We are currently at 77% recruitment for year 1, and on target to meet anticipated year 1 recruitment in February 2015.

Phase 1 Pilot:
The exploratory measures were piloted alongside original scales from January – May 2014 in London, Newcastle and Rome.

40 non-ambulant patients were assessed with the novel scales aged 2 to 24 years. Preliminary modern psychometric analysis identified good item fit for both scales. Regarding the exploratory HFMS, the need to test the more difficult items in the ambulant population was identified.

The methodology described in Figure 2 was applied to both scales and a phase 2 pilot recommended with a larger cohort and wider spectrum of abilities.

Phase 2 Pilot:
Following phase 1, the exploratory HFMS was further revised, this included the addition of items from the North Star Ambulatory Assessment to remove any ceiling effect. This exploratory scale was renamed the Revised Hammersmith for SMA (Draft) and now consists of 30 items covering assessment of motor abilities in SMA types 2 & 3. See Figure 3 for the current proforma.

The RHS (Draft) is being prospectively tested alongside the original HFMS and NSAA in:
- UK: London & Newcastle
- Italy: Rome
- US: Columbia University & Boston Children’s

The same sites are also piloting the revised Upper Limb Module for SMA (ULM2).

Phase 2 is due to be completed on 15/10/2014 with anticipated discussion of clinical trial readiness of both scales at the forthcoming SMA EHMC workshop in November 2014.

In the UK the PEDI-CAT for SMA is also being piloted as a patient reported outcome measure in collaboration with the work being undertaken by Amy Pasternak and colleagues in the US.

Conclusions:
An international collaboration between SMA REACH UK, the Italian SMA Network and the PNCR for SMA have made a commitment to improve the scales in SMA. Early findings using modern psychometric analysis from a small cohort of SMA patients has identified promising early feedback on the exploratory scales. We await the end of the second phase of the pilot prior to reporting more formally on their clinical trial readiness.

These scales will require further testing with modern and traditional psychometric techniques on a larger cohort of patients. Future work as part of this study will address functional scales in type 1 SMA, and the use of patient/parent reported outcome measures in SMA.

This collaborative work will be an invaluable tool for centres likely to be involved in upcoming multicentre randomised controlled trials in SMA in addition to use in the routine clinical setting.

References:

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