



What is AmSMART?

Spinal muscular atrophy (SMA) is a genetic disease of the anterior horn cell with a frequency of 8 per 100,000 live births with high mortality during infancy. There is no known treatment for SMA. Until recently, no therapeutic trials have been attempted and, then, only adult patients were included. The AmSMART group is an organization of 15 pediatric medical centers and the Center for Biostatistics and Clinical Science at UT Southwestern formed in order to perform clinical trials in children with SMA. Funding has been through the National Institute for Neurological Disease and Stroke, National Institutes of Health. Because very little is known about the biochemistry of SMA, any benefit of proposed treatment could only be measured by examining the patient. Our first objective was to devise reliable methods to measure strength, motor function, lung function and quality of life to be used as outcome measures for clinical trials.

During 2001-2002, 12 children with SMA aged 2 to 14 years were enrolled for a reliability study of 4 outcome measures. Quantitative muscle test (QMT) was done in children greater than 5 years old using the Richmond Quantitative Measurement System. The Gross Motor Function Measure⁹ (GMFM) was used to measure muscle function in children beginning at age 2 years. Pulmonary function tests (PFT) were done with the KoKo⁹ system in children at least 5 years old. Finally, the group worked with an established Quality of Life (PedsQL⁹) tool and designed an adjunctive questionnaire to address issues pertinent to children with muscle weakness. The Richmond Quantitative Measurement System (RQMS) was used to test grip, knee flexion and extension, and elbow flexion. All testing was done by trained "evaluators" (physical therapists). 10 children fulfilled inclusion criteria and completed at least 3 visits with 3 evaluators over a 6-month period. GMFM showed high inter-rater reliability. QMT showed greater variability among the weakest children compared to stronger subjects. The Peds-QL Neuromuscular Module for parents was found to have moderately high reliability. This part of the project was completed in Dallas. Upon completion of the first reliability study, evaluators were ready to begin seeing patients at their respective medical centers. In 2002, 38 children with SMA were enrolled at 5 pediatric centers. Each was seen at least 3 times. Thirty-four patients and 7 evaluators completed the study. Thirteen patients were aged 2 to 5 and 21, 5 to 18 years. Gross Motor Function MeasureTM (GMFM) was completed by 34 subjects. Six parameters for Pulmonary Function Tests (PTFs) were measured in 20 subjects. Quantitative muscle testing (QMT) was performed on 21 subjects in 8 muscle groups. Thirty-three subjects completed the PedsQLTM (QOL) Neuromuscular Parent module. After careful statistical analysis, we concluded that the Gross Motor Function MeasureTM, Pulmonary Function Tests, Quantitative Muscle Testing and Quality of Life are reliable outcome measures for children with SMA. These results show that our methods have "intra-rater" reliability and can be used with confidence in a clinical (drug) trial. Thus, in 2002, we began a randomized, double blind trial of creatine. Children with SMA who were at least 2 years old have been followed at the 5 centers. Enrollment closed

March 1, 2003. More than 50 patients completed the study by December, 2003. The statistical analysis is ongoing and should be complete by in March, 2005. We applied for, and received, continued funding from NIH and from the Muscular Dystrophy Association. We have expanded AmSMART to include more pediatric centers around the US and in Canada.



We have the current studies underway at our  centers:

AmSMART is seeking infants with SMA type 1 for an open label pilot trial of Riluzole (Rilutek™). Child must have genetically confirmed diagnosis of SMA (SMN deletion); 0 to 24 months of age; not able to sit independently for greater than 10 seconds when placed; not on mechanical ventilation of any kind for greater than 16 hours/day. Log onto www.amsmart.org for additional information.

AmSMART is seeking children with SMA to participate in a Quality of Life (QOL) reliability and validity study. Caregiver and child modules will be given at each of 2 visits. Child must be at least 2 years old, but should not have reached 18 years of age at time of enrollment; must not be on mechanical ventilation of any kind for greater than 16 hours/day. Log onto www.amsmart.org for additional information.

In this way, we hope to be able to include infants with SMA as well as other patients who are unable to travel in future clinical trials. We are hopeful that new drugs will become available for testing in the next few years and we are confident that our methods of testing the effects of those drugs will be reliable and accurate.

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