3.3% in SMA2 and 1.8% in SMA3. In SMA2, FVC %pred. declined steeply from 5 to 15 years of age, followed by a levelling. Conversely, in SMA3 patients FVC %pred. declined slower but steadily from 10 years of age. In SMA2 FVC% pred. significantly positively correlated with HFMS and RULM ($r=0.60$, $p<0.01$ and $r=0.55$, $p<0.01$) as in SMA3 ($r=0.7$, $p<0.001$ and $r=0.6$, $p<0.01$). Recumbent length or ulnar length were used as surrogate for height in FVC %pred. calculation in SMA2. The results of this ongoing collaborative work suggested that in SMA2 and 3 lung volumes decline from age 5 and 10 respectively. Lung and motor function correlate well both in SMA2 and 3. This data will help the assessment of the long-term efficacy of treatment for SMA.

http://dx.doi.org/10.1016/j.nmd.2019.06.337

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Supportive thoraco-lumbar-sacral orthosis (TLSO) provision for spinal muscular atrophy (SMA) type 1 children treated with nusinersen

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Spinal muscular atrophy (SMA) is a genetic neuromuscular condition, caused by loss of SMN1 gene resulting in reduced SMN protein with degeneration of motor neurons in the anterior horn. In its most severe form (SMA type 1) children present with weakness before 6 months. Prior to the development of treatment, children never achieved the ability to sit, typically dying by age 2 years. Nusinersen, an antisense oligonucleotide, increases the production of SMN protein by the SMN2 gene, with improved motor function. SMA 1 children treated are living longer, attending nursery / school. They are spending more time in an upright position (supported by wheelchairs / seating) as well as some achieving independent sitting and skills which were previously impossible. This study aims to evaluate the effect of improved function and sitting on their spines and management options. Routine assessment (with consent from families) of 30 SMA children on Nusinersen, aged 2 months to 9 years old, at Great Ormond Street Hospital commonly showed spinal asymmetry either at rest or when sat and was noted as young as 4 months in a patient. This necessitated provision of supportive thoraco-lumbar-sacral orthosis (TLSO) in over 70% of children with the aim to slow progression and need for spinal surgery. One child did not tolerate sitting therefore a TLSO has not been implemented and another was too severe for casting. TLSOs have further been used to help children practice sitting with more support. No deaths have been recorded in this SMA 1 group in the last 2 years, where previously they would have a palliative approach to their care with minimal physiotherapy input. This study shows the importance of early monitoring and proactive management of spinal asymmetries in children with SMA 1 on nusinersen. With this increasing population further consideration is needed to early and ongoing assessment of these patients. They need proactive physiotherapy management for new and developing challenges.

http://dx.doi.org/10.1016/j.nmd.2019.06.338

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Reducing the diagnosis time of neonatal screening by optimizing the screening process: the southern Belgian experience

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Newborn screening (NBS) of spinal muscular atrophy (SMA) started in southern Belgium in March 2018. Initially covering the annual 17,000 births from the Liege Center, the program gradually expanded to 3 screening centres and currently covers 60,000 births per year. In NBS, turnaround time is critical. The aim of this report is to examine the effect of actions conducted to decrease it. During the first period, from March to December 2018 (13,000 newborns), results were available within 15.35.0 days (meanSD) after birth. Dried blood spots (DBS) were delivered to the screening lab within 3.12.9 days, and analysis was performed within 83.5 days. Altogether, 90% and 99% of results were available within 12.2 and 21.3 days after DBS reception, respectively. In order to decrease this delay, we conducted 5 actions that were fully operational on January 01st. We developed and validated new primers for the qPCR method, in order to increase robustness and avoid repeating runs. We hired a full-time technician specifically devoted to the project and conducted a training of the whole screening staff in order to ascertain that out of office periods are always and fully covered. We purchased and commissioned a new qPCR device, only devoted to SMA screening We optimized the DNA extraction protocol, reducing the number of manual handling steps. We extended the neonatal screening program to whole Southern Belgium, with the addition of 40,000 sample/year from 2 other Brussels centers. DBS are punched in each lab and sent to Liege central lab, which allows having daily instead of weekly runs. These improvements led to a significant drop of 2 days (6.12.5) in the average time of results reporting. 90% and 99% of results are available within 9.3 and 11.6 days, respectively. Optimization and upscaling in the screening lab may thus significantly decrease screening delays. To further decrease turnaround time, we also plan to automatize the extraction and qPCR processes.

http://dx.doi.org/10.1016/j.nmd.2019.06.339

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Longitudinal study of the natural history of spinal muscular atrophy type 2 and 3

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Spinal muscular atrophy (SMA) is characterized by the degeneration of the cells of the anterior horn of the spinal cord, causing muscle weakness and progressive atrophy. Characterize the natural history of patients with SMA type II and III to obtain more information about the clinical course. Prospective observational study of patients with SMA II and III. Patients were evaluated every 6 months for a period of 3 years. We collected demographic, clinical and genetic data. For the clinical evaluation, 3 standardized scales of motor function were performed: Hammerrsmith Funtional Motor Scale Expanded (HFMSE), Upper Limb Module Revised (RULM), Sixt Minute Walking Test (6MWT) and Egen Klassifikation 2 (EK2). The patients were classified into different groups depending on the type of SMA. We have 3 years follow-up in 19 patients SMA II and 5 patients SMA III and 2 years follow-up in 32 patients SMA II and 14 patients SMA III. In SMA II patients, corrected for age, a significantly higher average score was found in the motor function scales in patients with SMA IIb. Similar results were found in patients with SMA III, with better values in patients IIIb. In 2 years follow-up in SMA II patients younger than 6 years show an increase of +1.5 in HFMSE and +1.6 in RULM. In older than 6 years show a decrease of -2 in HFMSE and -0.9 in RULM. Motor function normalized by age is better in AME IIb than in AME IIa. Similarly, in AME IIIb than in AME IIIa. The age of AME II patients should be taken into account in the analysis of the response to new treatments. Patients younger than 6 years show a different trajectory in the progression of the disease than older patients.

http://dx.doi.org/10.1016/j.nmd.2019.06.340
