SHORT COMMUNICATION

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Comprehensive assessment model for patients with spinal muscular atrophy: proposal of tools for clinical practice and real-world studies

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Spinal muscular atrophy (SMA) is a rare genetic condition, with an incidence of 10 per 100,000 live births, in which an autosomal recessive alteration occurs in the motor neuron survival gene *SMN1*, leading to hypotonia, progressive weakness, developmental damage, and motor losses[1].

It is a condition with great variability in presentation and clinical course, classified into four types from I to IV based on the age of onset of symptoms and maximum motor function reached, with type I, with childhood onset, being the most severe and type IV, with late onset, having a better prognosis. Type I SMA affects infants before 6 months of age, impairs the acquisition of motor milestones, and reduces life expectancy[1]. The severity of the disease and its limitations are related to complications of the respiratory, musculoskeletal, cardiovascular, and gastrointestinal systems[2,3].

Advances in elucidating the molecular, cellular, and physiological processes of disease have allowed innovative studies with disease-modifying therapies, in combination with interdisciplinary care, that demonstrated promising results in clinical trials and real-world studies[1-3].

Among the three alternatives approved as disease-modifying therapies, Nusinersen, an antisense oligonucleotide, increases the production of the motor neuron survival protein by acting on the inclusion of exon 7 in the mRNA transcripts of the *SMN2* gene. It is a medication applied via intrathecal administration with four loading doses on days 0, 14, 28, and 63 and reinforcement every 4 months[1,4]. Safety and efficacy research and real-world studies demonstrate positive results and suggest new phenotypes[1]. However, differences in study methodologies in different countries may limit of results and indicate the need for greater standardization in evaluation[4].

The interpretation of real gains of the patients is impaired by the heterogeneity of the studies, different periods of data collection, and duration of follow-up, as well as by the use of different outcome measures and poor description of quality of life, respiratory, and nutritional outcomes[1].

A recent systematic review shows an important gap in the follow-up data of the therapeutic program of children with SMA I and highlights the need for new studies with independent publication, without conflicts of interest, that reinforce the long-term stabilization of results, functional abilities acquired, and additional characteristics of patients and multidisciplinary therapies[4].

As it is an expensive drug, such data and information reaffirm its cost- effectiveness and guarantee the treatment. In Brazil, the drug was incorporated in 2019 for patients with SMA I. The new Clinical and Therapeutic Protocol, approved in January 2022, brings recommendations for the analysis of clinical effectiveness, including the use of the Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders (CHOP INTEND)[5], Hammersmith Infant Neurological Exam-Part 2 (HINE-2)[6], and Expanded Hammersmith Functional Motor Scale (HFMSE)[7], and also the evaluation of time/modality ventilation, invasive or noninvasive (NIV), oral or alternative feeding, and anthropometric measurements[8].

There is a lack of scientific publications about Brazilian patients undergoing treatment. One study showed an increase in the CHOP INTEND score of more than 70% of the 21 patients using Nusinersen and the acquisition of new motor steps by 28% of them (cervical control and acquisition of sitting), and also reported a reduction in NIV time, corroborating data from international publications and contrasting with

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the natural history of the disease of losses, functional limitations, and early death[9].

We did not find reports demonstrating the experience of other reference services, with detailed information and a more comprehensive and long-term approach of the observed effects. There is also a question about the determination of factors that may also influence the results, in addition to the number of copies of *SMN2* and the precocity of treatment, such as performing therapies, contractures, and preexisting deformities[4].

In view of this limitation of data and correlations and based on international care recommendations and subsequent publications, we suggest an initial evaluation model supplementary to that proposed in the Clinical Protocols and Therapeutic Guidelines for the follow-up of patients with SMA type I using Nusinersen. The aspects that require further investigation and indicated measurement instruments are presented in Table 1.

As it is a multisystemic condition, there is a need for a comprehensive investigation, considering several biopsychosocial aspects[2,3]. The choice of the best tool should consider the child's age and collaboration, as well as the evaluator's knowledge regarding the criteria, application methods, and clinical implications of the findings. In our routine, patients are always evaluated before applying the next dose of medication, up to a maximum of 7 days in advance.

To verify motor function, it is recommended that the CHOP INTEND scale be used with all patients under 2 years of age and with those over 2 years without the ability to sit. The HFMSE is intended for children over 2 years of age who sit or who have a CHOP INTEND score greater than 60. In cases of scores between 50 and 60 on the CHOP INTEND, both scales must be applied. The HINE-2 should be used on patients aged up to 2 years[10].

During the respiratory assessment, not only the time of use of NIV and oxygen pulse saturation should be recorded but also aspects such as the presence of a paradoxical thoracic pattern, growth and development of the rib cage, nocturnal oximetry, lung volumes and capacities, and cough effectiveness need to be measured. These parameters also indicate the adequacy of ventilatory support levels, changes in patient autonomy, and the necessary level of assistance, which allow for better longitudinal follow-up and therapeutic programming[2,11].

The Great Ormond Street Respiratory Score for SMA I (GRS) is also a current alternative to quantify stability and need for assistance[11]. The choice for low- and/or high-cost resources, such as plethysmography, sniff nasal inspiratory pressure, and diaphragmatic ultrasound, will depend on the availability of the service.

The observation of dietary aspects is also relevant, especially with regard to nutritional adequacy and risk of bronchoaspiration, occurrence of fatigue during oral feeding, and regurgitation. The Oral and Swallowing Abilities Tool was developed for this purpose[12]. In specific cases, a study of swallowing by videofluoroscopy can also be performed.

The observation of cognitive and communication aspects allows demonstrating the child's interaction with the environment and improving educational strategies and socialization[13]. It is also interesting to assess quality of life and caregiver burden[14].

The clinical state of the patient must be described in all evaluations, including the presence of pain, contractures and deformities, previous or concomitant diseases, medications, occurrence of dysautonomia, and indication for cardiological evaluation[2,3].

Table 1. Proposed tools for evaluating patients with type I spinal muscular atrophy.

Involvement	Aspect	Assessment tools
Motor	Motor function Motor developmental stages	CHOP INTEND[5] e HMFSE[6] HINE-2[7]
Respiratory	Rib cage growth	Chest circumference[15]
	Vital capacity	Ventilometry[16]
	Sleep disorders	Nocturnal oximetry, poly/polysomnography[17]
	Inspiratory pressure	Sniff nasal inspiratory pressure (SNIP)[18]
	Cough effectiveness	Cough peak flow[19]
	Diaphragmatic mobility and thickness	Diaphragmatic ultrasound[20]
	Ventilatory pattern	Plethysmography[21]
	Stability and need for support	GRS Score[11]
Nutritional	Deglutition	OrSAT[12] Swallowing videofluoroscopy

CHOP INTEND: Children's Hospital of Philadelphia Infant Test of Neuromuscular Disorders; HINE-2: Hammersmith Infant Neurological Exam-Part 2; HFMSE: Expanded Hammersmith Functional Motor Scale; GRS: Great Ormond Street Respiratory Score for SMA1; OrSAT: Oral and Swallowing Abilities Tool.

We emphasize the importance of proactive multidisciplinary rehabilitation care, which must be included in the individual therapeutic protocol of patients with the participation of the family. There is a demand for training professionals to assess and treat patients, favoring early diagnosis and intervention, minimizing complications, and ensuring the achievement of the maximum potential of each child with SMA.

AUTHORS' CONTRIBUTIONS

LBA: Conceptualization, Writing – original draft, Writing – review & editing. **VVDL:** Conceptualization, Writing – original draft, Writing – review & editing. **RMRA:** Conceptualization, Writing – original draft, Writing – review & editing.

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