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Research Article

Respiratory Improvements in Type 1 Spinal Muscular Atrophy Treated with Disease-Modifying Therapies: An Observational Study

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Abstract

Introduction: Spinal muscular atrophy (SMA) is a genetic disease with homozygous deletion or mutation of the SMN1 motor neuron survival gene. Incidence is 1 in 10,000 births. Clinical manifestations include variable progressive muscle weakness, respiratory and bulbar muscle involvement, respiratory failure, dependence on noninvasive ventilation (NIV) or tracheostomy tubes (TQ) with normal cognitive development; about 50% are SMA type 1. In 2017, specific molecules emerged that increase SMN protein through messenger RNA splicing modifications or gene therapy, improving motor function. Data on respiratory outcomes are limited, the main cause of premature death or morbidity.

Objective: To describe the ongoing respiratory status of children with SMA1 treated with specific therapies at a national referral center in Chile.

Method: Prospective cohort of SMA1 patients treated at the neuromuscular disease program at Clinica Las Condes, Santiago, Chile 2017 to 2022. A respiratory care guideline for ventilatory failure prevention was developed, with early noninvasive ventilatory support (NIVS), high IPAPs (14 to 18) and low EPAPs (3-4), differential 10-15, nasal interface, plus pulmonary recruitment with cough assistance equipment and/or ambu bag. Approved by Institution Ethics Committee 2017. Respiratory support and complications were recorded until 2024.

Results: Thirty-three SMA1 patients receiving treatment were recruited: nursinersen 28, risdiplam 4, gene therapy 8, and combination therapy 7. The median age at diagnosis was 2 months (0-10), and the median current age is 36 months (4-94); 48% (16/33) were admitted with TQ for follow-up and are still on it, one patient died. 18 patients were admitted without TQ, started with early NIVS; one on presymptomatic treatment never used NIVS: 50% (9/18) with NIVS achieved sitting position and 2 were able to walk. Four patients were intubated, one of them was successfully extubated on 3 occasions. Children without TQ use NIV at night and during respiratory infections. Twenty-seven hospitalizations were recorded in 11 patients; 2 patients have chronic atelectasis at start of protocol. None develop chronic atelectasis during protocol follow up.

Conclusion: Despite specific therapies improved motor function, patients with TQ at the beginning of the study are still on it. Patients without TQ at baseline have been unable to discontinue NIVS, but they require same o less support, with shorter hospitalizations and complications. Starting specific therapies presymptomatic o very early in the course of the diseases have better motor and respiratory outcomes, however NIVS is crucial to have less respiratory complications and medical resource utilization.

Keywords: *Spinal Muscular Atrophy; Respiratory Care; Non-Invasive Ventilation; Non-Invasive Ventilatory Support; Nursinersen; Risdiplam; Gene Therapy; Onasemnogene Abeparvovec*

Introduction

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease that causes progressive death of motor neurons originating in the spinal cord and bulbar region, with consequent muscle weakness. It is the leading genetic cause of mortality in infants, mainly due to respiratory complications. Its incidence is 1 in 10,000 births and prevalence is 1-2 in 100,000 individuals. This disease results from a homozygous deletion or mutation of the motor neuron survival gene SMN1, located on the long arm of chromosome 5 [1-3]. Currently, in some countries, it is diagnosed early through neonatal screening and even prenatal diagnosis [4]. Clinical manifestations have a wide spectrum of severity in relation to the degree of muscle weakness, which primarily affects the extremities and, to a variable extent, the respiratory and bulbar muscles, with normal cognitive development. Although the severity of clinical manifestations in SMA is recognized as a continuum, four main subtypes have been defined in the pediatric population. In SMA type 0, which begins prenatally, patients present with no respiratory effort at birth, require ventilation, and lack motor activity. They typically die within the first few weeks of life. SMA type 1 occurs in newborns and infants and is unable to sit; SMA type 2 patients are unable to walk but are able to sit; and SMA type 3 patients are able to walk independently [1-3,5]. Patients with SMA type 1, also known as Werdnig-Hofmann disease, represent approximately 50% of all SMA types. 1 In these patients, the natural history of the disease shows that they die before 24 months of age due to respiratory failure, with an average survival rate between 6 and 9 months [4].

This reality has changed substantially in recent years, primarily due to the increase in preventive and proactive clinical care, associated with a greater understanding and knowledge of SMA [2,3,6,7]. The prognosis for these patients has significantly improved with the incorporation of nutritional and respiratory support, as proposed in the expert consensus statement on standard care for patients with SMA [2,3,7]. An increasing percentage were living beyond the age of 2, thanks to the introduction of early non-invasive ventilation (NIV), gastrostomy, and the use of a mechanical in-exsuflator (M-IE) or cough assist [1-3,6,7]. We are currently facing a significant change in the way we understand SMA, due to the rapid development of various specific therapies that have radically changed what we knew as the natural history of this disease [8,9]. These specific disease-modifying treatments include new, highly specific molecules for increasing the SMN protein through messenger RNA splicing modifications or gene therapy [8,9]. In December 2016, the FDA approved the use of nusinersen (Spinraza^{R}) for intrathecal use in patients with SMA, the first specific therapy to modify the natural history of SMA. In 2019, the oral therapy Risdiplam (Evrysdi^{R}) was incorporated for children over 2 months of age, both therapies aimed at increasing the SMN2 protein [8,9]. The SMN1 gene replacement therapy, onasemnogene abeparvovec (Zolgensma^{R}), was approved in 2019 for all children with SMA under the age of two years, without terminal weakness [8,9]. These drugs clearly improve motor function, with less evidence of respiratory outcomes [10,11]. Historically, clinical trials used as outcome measures, approximately 16 hours of noninvasive ventilation (NIV) or tracheostomy ventilation (TQ). However, the robustness of this endpoint has been questioned, as it relies on parental report or physician choices that influence treatment [10,11]. Clinical trial results suggest improved survival and ventilatory support; however, other studies investigating respiratory muscle function in SMA1 conclude that, while Nusinersen may improve respiratory function, it does not eliminate the need for NIV and bag-assisted recruitment maneuvers or M-IE cough aid to prevent respiratory failure [12]. It has been difficult to assess the respiratory status in children with SMA1 on specific treatments. Many scores have been developed [13]. Our objective was to describe the respiratory status follow up of SMA1 patients receiving comprehensive care, including disease-modifying treatment and proactive respiratory management from diagnosis onward at a referral center in Chile.

Method

A prospective observational cohort study of patients with SMA type 1 treated in the neuromuscular disease program at Clinica Las Condes between 2017 and 2023. Patient registration follow up was approved for research and report purposes by Clinica Las Condes Ethics Committee on January 20, 2017. Informed consent was requested from the patients' legal guardians for their participation in the study.

Patients: SMA 1 patients of varying ages and disease progression were evaluated, some already with ventilation through tracheostomy (TQ) and others recently diagnosed. Patients requested evaluation by our multidisciplinary team. Local management guidelines developed in accordance with international guidelines were systematically applied [1-3,7,14]. Patients were evaluated with a multidisciplinary team with functional scales, biomarkers, and clinical assessments, including respiratory support. In patients without TQ and/or recently diagnosed, noninvasive ventilatory support (NIVS) was started as soon as possible in all SMA 1 patients, when presence of paradoxical breathing was observed, in order to prevent respiratory failure related to viral infections, maintain rib cage support to minimize micro-atelectasis formation, and allow for proper chest development. We do not waited for sleep study to initiate the NIVS. We do no waited for sleep study to initiate de NIVS included airway recruitment through the use of an ambu bag which was started preemptively from the first day of consultation and/or mechanical in-exsufflation M-IE. This was continued two to three times a day, pending the availability of ventilation equipment and the prompt initiation of NIV, in order to acclimatize the patient and prepare them for potential viral infections. This was achieved through a nasal interface-pediatric wisp- with a silicone cushion and minimal contact, allowing infants and children to use it in their daily activities. Preventive NIV was initially administered in S/T mode with high IPAP (14 to 18) and low EPAP 3-4, with a span at least 10 to 15. Adjustments were generally made on an outpatient basis. Some patients were started on NIV while hospitalized in another center, in an intensive care unit, with total-face interfaces. A total-face mask interferes with oral suction, help to accelerate de loss of swallowing and alters drooling management. Once MI-E was available, parents were progressively trained in its use to maintain rib cage support [15]. The pressures used were progressively increased until reaching at least +/- 40-50 cm H_2O and its use was recommended 2 to 3 times daily, pending on chest wall collapse. Our experience with the use of the M-IE in infants less than 2 years of age began in 2010. Parents were trained to recognize the risk of acute ventilatory failure, especially in relation to the onset of viral infections, which is very important for the airways recruitment and facilitation of coughing in respiratory infections, in order to prevent atelectasis. Oxygen saturation measurement was instructed, and the use of the MI-E was recommended to be increased to 3 to 4 times daily in the case of viral outbreaks [15].

Feeding: We attempted to keep oral intake, ideally breast fed, in order to maintain suction and swallowing, avoiding accelerated loss of feeding function. Weight growth was monitored, avoiding malnutrition. In patients with sialorrhea, with evident swallowing disorders, poor weight gain, or in cases of doubt, a nasogastric tube or a gastrostomy was inserted to prevent aspiration into the airway. Gastroesophageal reflux and constipation were actively managed.

Statistical analysis: Descriptive statistics were used for demographic and clinical variables of all patients. The sample size was considered to be the total population of patients evaluated by our team during the period analyzed. Proportions, measures of central tendency, and dispersion were calculated. Continuous variables were treated according to normal distribution, using the mean and standard deviation, and in the case of variables with abnormal or skewed distributions, the median and standard deviation were used.

Results

Thirty-four SMA 1 patients were evaluated, with a median disease diagnosis of 2 months (0-10). The median evaluation time at the cutoff of this follow-up (2024) was 24 months (4-88). The specific therapies received were nursinersen in 28 patients, risdiplam in 4, and gene therapy in 9, with 7 receiving combination therapy.

SMA 1 patients with TQ: 47% (16/34) entered follow-up and began specific therapies with chronic ventilation through TQ. One patient with TQ died at age 7. None discontinued TQ during the follow-up period. One of them achieved sitting.

SMA 1 patients without TQ: 53% of children (18/34) entered follow-up without TQ; 72% (13/18) started on NIVS with MI-E and/or ambu bag during their initial consultations. Table 1 shows the demographic and clinical characteristics of the patients without TQ, including treatment type. Currently, 61% (11/18) are using NIVS, maintaining the preventive use of lung recruitment with MI-E and/or ambu bag. Two patients require NIVS only during exacerbations. One patients SMA 1c who received gene therapy, currently is ventilated

only at night through TQ due to a severe respiratory infection that required intubation with a failed extubation. This patient had asthma as an associated comorbidity. A patient who started treatment pre-symptomatically, whose early diagnosis was made because she has a brother with SMA type 1 and TQ, never used NIVS. Patients without TQ, 9/18 (50%) were able to sit, and two patients are now walking. The children use NIV at night and during respiratory exacerbations as a preventive measure. Before starting NIV, all patients had a flared chest, with the chest circumference at the nipple less than the lowest chest circumference, which was corrected with NIV. Few patients had a normal sleep study, with already paradoxical breathing. The best chest support and the least paradoxical breathing occurred in those infants who used MI-E, rather than ambu bag (Table 1).

Patients	AME 1 Type	Nº Copies	Treatment 1	Treatment 2	AGE at diagnosis	Actual age	Motor milestones achived	Feeding	NIVS	NIV > 16 h	MIE
1	1c	2	NURS		9 m	7a 4 m	No	GTT	Yes	No	Yes
2	1b	2	NURS	TG	4 m	3a 4m	Sitting	GTT	Yes	No	Yes
3	1a	2	NURS	TG	17 days	2a 10 m	Walking	Oral	Yes	No	Yes
4	1b	2	TG	NURS	3 m	2a 11 m	Sitting	Oral / NG tube	Yes	No	Yes
5	1b	2	NURS		1 m	2a	Sitting	Oral	Yes	No	Yes
6	1b	2	NURS		2 m	1a	Sitting	GTT	Yes	Yes	Yes
7	1b	2	NURS	TG	1 m	1a 10m	Sitting	Oral	Yes	No	Yes
8	1b	2	NURS		3 m	1a 11m	Sitting	GTT	Yes	No	Yes
9	1b	2	NURS	TG	2 m	4m	No	Oral	Yes	No	Yes
10	1b	2	NURS		3 m	1a 8m	Sitting	Oral / SNG	Yes	No	Yes
11	1b	2	NURS	TG	2 m	4a 7m	Sitting	GTT	Yes	No	Yes
12	1b	2	NURS		2 m	2a	Sitting	Oral / SNG	Yes	No	Yes
13	1c	3	RISD		10 m	3a 8 m	No	Oral	Viral Infections	No	No
14	1b	2	RISD		6 m	3a 7 m	No	Oral	Yes	No	Yes
15	1b	2	TG	RISD	1 m	5a 2 m	Walking	Oral	No	No	No
16	1c	2	RISD		2 m	5a 7 m	Sitting	Oral	Yes	No	No
17	1c	3	TG		8 m	2a m	Sitting	Oral	No	No	Yes
18	1c	2	TG		6 m	3 a 5m	Sitting	GTT	TQ	No	Yes

Table 1: *Clinical, demographic characteristics and respiratory status in patients with spinal atrophy type 1 without tracheostomy at the begining of treatment. Clinica Las Condes 2017-2023.*

GT: Gene Therapy; NURS: Nursinersen; RISD: Risdiplam; NIV: Non Invasive Ventilation; M-IE: Mechanical In-exsuflator; GTT: Gastrostomy.

Respiratory infections in patients without TQ: Many patients were saved from an acute lung collapse with the use of M-IE. A total of 27 hospitalizations has been recorded so far in 11 patients, with an average of 1.5 hospitalizations per patient. Most of them were for observation for 1 to 2 days; two patients with no MI-E at home had prolonged hospitalization. Only two patients had chronic left lower lobe atelectasis, one of them total. Average of hospital admission were 3 days.

Intubations and extubation: Four patients were intubated for severe respiratory infections and atelectasis, and were successfully extubated. The Bach protocol, incorporated into local management guidelines, was used [1,14,16,17]. This included extubating to a nasal interface (pediatric nasal wisp), which allows a better management of frequent sialorrhea, NIV with high support with a differential of 14 to 18, high IPAP and low EPAP of 3-4, in addition to the frequent use of a cough aid before and after the procedure. The spontaneous ventilation test for classical extubating protocol was not used. One of the patients was hospitalized and intubated three times, all with successful extubation to NIVS. This patient had a previous right lower lobe atelectasis and bronchial hyperreactivity that complicated respiratory management.

Discussion and Conclusion

This is the first Chilean and Latino-American study to report the prolonged respiratory status of a large cohort of SMA type 1 patients receiving specific therapies. The natural history of SMA type 1 has shown that patients die before 24 months of age due to respiratory failure, with a median survival rate between 6 and 9 months. Given the incorporation of therapies that modify the natural history of SMA [8-12], which are very expensive, we decided to report the respiratory outcomes of 34 patients with SMA type 1 receiving specific treatments. Not all patients started treatment early, and just under half already had TQ at the time of starting treatment. The most severe forms of SMA, Werdnig Hoffmann disease or SMA type 1, present with alterations in ventilation, impaired cough capacity due to the absence of the cough reflex and swallowing disorders. The compromise of the ventilatory pump, with decreased lung volumes, vital capacity and inspiratory reserve, associated with the absence of sighs, favors the formation of micro-atelectasis and the increased risk of alveolar hypoventilation. Coughing incapacity hampers the mobilization of secretions from the distal airways, further increasing the risk of atelectasis and/or pneumonia [1].

Our follow-up protocol, especially in patients without TQ, included early initiation of NIVS (NIV + IE-M and/or bag-assisted ventilation) in all patients with paradoxical breathing in a preventive approach. This has improved survival prior to therapy [16], in accordance with reports in clinical trials [10-12] and by Bach [3,16]. In our experience, this approach has prevented respiratory failure in many patients and, even more so, avoided hospitalization and intubation, with the consequent risk of requiring ventilation through TQ. We did not wait for a sleep study, because in our previous experience with normal results babies did collapse with viral infections. Each respiratory event means a setback in motor skills and swallowing, in addition to nutritional compromise. In these children, minor respiratory infections cause the onset of respiratory failure due to hypoventilation and the formation of atelectasis leading to global respiratory failure [1,5]. If there is also airway aspiration or bronchial hyperreactivity and/or asthma, the management of respiratory infections are even more difficult. The use of bronchodilators, combined with conventional physical therapy without performing lung recruitment maneuvers and manual and/or mechanical cough facilitation, are common errors. Also, chest support has been more successful when using an MI-E over ambu bag [15].

In our experience, to prevent TQ, it is essential to have the elements of NIVS in place, extubating to NIV with high support or high span, with high IPAP and the lowest possible EPAP to facilitate CO_2 elimination, in stable patients without fever or oxygen requirements, requiring MI-E physiotherapy no more than 3 times a day, extubating to a nasal interface, which allows the management of sialorrhea, a very bothersome problem in these patients [1,14]. This same approach is proposed by Bach and Al-Subu AM [16-18].

SMA 1 patients should be incorporated into specific therapies before they experience complications, ideally without TQ. Our study included 16 patients who were already on TQ when they started their treatment; none have been extubated to date. This is possibly because many of them started treatment late. Decannulation of children with SMA type 1 requires patient cooperation, as reported by Bach [16]; therefore it is important to avoid TQ in patients undergoing treatment. Chilean natural history studies report a high frequency of chronic ventilation through TQ in SMA type 1 patients in the AVNI-AVI (Non-Invasive Ventilatory Assistance - Invasive Ventilatory Assistance) program of the Ministry of Health (MINSAL) [19]. Using these noninvasive respiratory support actively, patients can also be successfully treated for respiratory exacerbations, avoiding endotracheal intubation.

The new Great Ormond Street Respiratory (GSR) scoring system was developed for the assessment of more objective and standardized respiratory outcomes in children with spinal muscular atrophy type 1 (SMA1) receiving specific treatments, without TQ. The GSR score allows monitoring of respiratory function using an objective tool, since it reflects the level of respiratory care required by patients with SMA1, and authors recommend to be used in combination with the clinical history and presentation [13]. The performance of this score was evaluated and its contribution to our center was modest, given that our approach to patients was preventive and proactive. The criteria for initiating ventilatory support, with early NIV and the use of cough assistance for rib cage support, were developed locally following management standards guidelines, and these criteria were applied at the time of initial consultation whenever possible. Comparison of GSR scores from different cohorts at different institutions is feasible, when the protocol is similar to the proposed by our group, with early timing of NIV initiation and MI-E.

We recognize that there is variation in practice in Chile and abroad, which limits the use of this score and other objective measures that allow monitoring of patient respiratory progress on these therapies at individual centers. The literature supports this management approach, with NIVS and MI-E. Our experience has been positive, as patients have a low rate of hospitalization and complications such as chronic atelectasis. In this series, not all patients were seen at our center during their hospitalizations. Upon hospitalization, patients were trained to accompany their equipment to manage respiratory failure during hospital admissions, avoiding endotracheal intubation and allowing a successful extubation, if necessary. Extubation protocols for patients with spinal muscular atrophy, especially those with SMA 1, are limited, and have been published with successful results [17,18,21]. However, over the years, intensivists have accepted the use of NIVS and MI-E, with appropriate pressures to normalize ventilation and oxygenation, with minimal PEEP/EPAP in S/T modes, combined with mechanical cough assistance before and immediately after extubation [21].

In summary, three treatments have emerged in the last six years-two drugs that modify exon splicing and one gene therapy-that have transformed the prognosis of this deadly disease. We are witnessing a paradigm shift in respiratory and pediatric care for patients with SMA. For new therapies to achieve the greatest effect on patients, it is essential to implement proactive multidisciplinary management that prevents the numerous medical complications of this progressive disease. International and local SMA care guidelines address respiratory, nutritional, and orthopedic management, the use of nutritional supplements, and the management of acute and surgical conditions in these patients [1,14,20]. We must organize ourselves as a country by optimizing early diagnosis and moving toward preventive management to avoid complications that will further impair quality of life, as they significantly contribute to the overall prognosis. Early NIVS in SMA1 prevents respiratory complications and avoids TQ, which will allow the child greater autonomy and better rehabilitation. The preventive use of recruitment maneuvers with M-IE and/or the use of nasal interface allows lung growth in the first years of life, age which is critical for lung development. It will be very interesting to evaluate long-term respiratory function in these patients, with progressive vital capacity measurement over time [21].

Conflict of Interest

The authors declare no conflict of interest.

Bibliography

1. Palomino MA and Castiglioni C. "Respiratory care in spinal muscular atrophy in the new therapeutic era". *Revista Chilena de Pediatría* 89.6 (2018): 685-693.

2. Mercuri E., *et al*. "Diagnosis and management of spinal muscular atrophy: Part 1: Recommendations for diagnosis, rehabilitation, orthopedic and nutritional care". *Neuromuscular Disorders* 28.2 (2018): 103-115.

3. Finkel RS., *et al*. "Diagnosis and management of spinal muscular atrophy: Part 2: Pulmonary and acute care medications, supplements and immunizations other organ systems and ethics". *Neuromuscular Disorders* 28.3 (2018): 197-207.

4. Dangouloff T., *et al*. "Newborn screening programs for spinal muscular atrophy worldwide: Where we stand and where to go". *Neuromuscular Disorders* 31.6 (2021): 574-582.

5. Swoboda KJ., *et al*. "Natural history of denervation in SMA: Relation to age, SMN2 copy number, and function". *Annals of Neurology* 57.5 (2005): 704-712.

6. Oskoui M., *et al*. "The changing natural history of spinal muscular atrophy type 1". *Neurology* 69.20 (2007): 1931-1936.

7. Sansone Racca F., *et al*. "1st Italian SMA Family Association Consensus Meeting". *Neuromuscular Disorders* 25.12 (2015): 979-989.

8. Fay A. "Spinal muscular atrophy: A (Now) treatable neurodegenerative disease". *Pediatric Clinics of North America* 70.5 (2023): 963-977.

9. Wang CH., *et al*. "Standard of Care. Consensus statement for standard of care in spinal muscular atrophy". *Journal of Child Neurology* 22.8 (2007): 1027-1049.

10. Finkel RS., *et al*. "Nusinersen versus sham control in infantile-onset spinal muscular atrophy". *New England Journal of Medicine* 377.18 (2017): 1723-1732.

11. Mendell JR., *et al*. "Single-dose gene-replacement therapy for spinal muscular atrophy". *New England Journal of Medicine* 377.18 (2017): 1713-1722.

12. Łusakowska A., *et al*. "Long-term nusinersen treatment across a wide spectrum of spinal muscular atrophy severity: a real-world experience". *Orphanet Journal of Rare Diseases* 18.1 (2023): 230.

13. Edel L., *et al*. "A new respiratory scoring system for evaluation of respiratory outcomes in children with spinal muscular atrophy type1 (SMA1) on SMN enhancing drugs". *Neuromuscular Disorders* 31.4 (2021): 300-309.

14. Palomino MA and Castiglioni C. "Atrofia Muscular Espinal: manejo respiratorio en la perspectiva de los recientes avances terapeuticos". *Revista Medica Clinica Las Condes* 28.1 (2017): 119-130.

15. Bach JR. "Prevention of precuts excavated for children with spinal muscular atrophy type I". *American Journal of Physical Medicine and Rehabilitation* 82.10 (2003): 815-819.

16. Bach JR., *et al*. "Changing trends in the management of end-stage neuromuscular respiratory muscle failure. Recommendations of an international consensus". *American Journal of Physical Medicine and Rehabilitation* 92.3 (2013): 267-277.

17. Bach JR and Palmieri JL. "A paradigm shift for the management of critically ill patients with spinal muscular atrophy". *Respiratory Care* 68.10 (2023): 1481-1482.

18. Al-Subu AM and Brazelton TB. "Management of critically ill patients with spinal muscular atrophy admitted with acute respiratory failure: The authors' reply". *Respiratory Care* 68.10 (2023): 1483-1484.

19. Karin Alvarez., *et al*. "Observations from a nationwide vigilance program in medical care for Spinal Muscular Atrophy patients in Chile". *Arquivos de Neuro-Psiquiatria* 77.7 (2019): 470-477.

20. Bach JR., *et al*. "Soporte respiratorio muscular para evitar el fallo respiratorio y la traqueotomía: ventilación no invasiva y técnicas de tos asistida". *Revista Argentina de Medicina Respiratoria* 2 (2013): 71-83.

21. Francisco Prado Atlagic., *et al*. "Respiratory care in patients with spinal muscular atrophy to avoid acute ventilatory failure and tracheostomy: literature review and consensus recommendations". *Neumología Pediátrica* 19.2 (2024): 49-58.

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