Sleep Medicine 86 (2021) 113–115

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Editorial

Paradigm shift in the era of disease-modifying therapies for Spinal Muscular Atrophy type 1: respiratory challenges and opportunities☆,☆☆

Keywords:
Spinal muscular atrophy
Nusinersen
Zolgensma
Noninvasive ventilation
Pulmonary clearance

1. Introduction

The era of precision medicine is upon us. Medical advances are improving the disease trajectories of many disorders and rapidly altering the practice of pulmonology. Spinal Muscular Atrophy type 1 (SMA1) is an autosomal recessive neuromuscular disorder caused by the degeneration of anterior horn cells in the spinal cord historically resulting in chronic respiratory failure and death by two years of life [1]. The disease trajectory is being modified by novel therapies including Nusinersen, Zolgensma, and risdiplam which have all been shown to improve motor-milestone response and survival [2–4]. Nusinersen is a landmark antisense oligonucleotide therapy [2] and risdiplam is a small molecule that both increase levels of SMN protein [5]. Onasemnogene abeparvovec, known as Zolgensma, is a single-dose gene replacement therapy [3]. However, disease-modifying therapies are noncurative in nature and patients often require ongoing supportive therapies including long-term mechanical ventilation, pulmonary clearance, and often enteral feeding [2,3,6,7]. The implementation of respiratory technology is complex in the real-world setting of overwhelming medical complexity and burdensome care plans that may lead to suboptimal therapy acceptance and adherence. Our aim is to describe the challenges associated with respiratory technologies in the era of SMA1 disease-modifying therapies to highlight opportunities for enhanced therapy acceptance and adherence.

2. Disease-modifying therapy challenges

Despite the clinically significant improvements conferred by disease-modifying therapies, treatment itself may be overwhelming and negatively impacted by the invasive nature of administration of some medications. Nusinersen therapy is noncurative and requires lifelong administration via repeated lumbar punctures with sedation. The loading dose phase includes four doses within two months followed by maintenance doses every four months. Both Zolgensma and Nusinersen administration may be negatively affected by the limited geographic distribution of treatment centers necessitating frequent travel to access care. Furthermore, financial barriers associated with the high price tag of disease-modifying therapies may also negatively affect access to treatment. Zolgensma has a staggering one-time cost of $2.1 million dollars, Nusinersen costs $750,000 for the first year followed by $375,000 annually thereafter [8], and risdiplam costs up to $340,000 annually.

3. Respiratory technology acceptance

Care plans that encompass daily treatment regimens, countless clinical visits with multiple healthcare professionals, and already burdensome treatments with disease-modifying therapies are time-consuming and complex. Although effective, the complexity of therapy programs may result in the inadvertent prioritization of disease-modifying therapies over supportive respiratory care. Furthermore, some patients and families may have the false impression that disease-modifying therapies provide a “cure” for disease, thus rendering noninvasive ventilation (NIV) and pulmonary clearance therapies obsolete in SMA1.

For children receiving disease-modifying therapy, the optimal timing of respiratory technology initiation remains somewhat unclear given the limited real-world experience of disease-modifying therapy effectiveness for sleep-disordered breathing and hypoventilation. This same uncertainty may lead to caregiver hesitance in pursuing respiratory technology, particularly because sleep-disordered breathing and hypoventilation have insidious onsets and may be clinically asymptomatic. Objective parameters via surveillance polysomnograms and/or other forms of gas exchange monitoring will help to inform these conversations. Of note, guidelines for the initiation of mechanical ventilation in the setting of this ‘new clinical trajectory’ is lacking for this population and is a needed area of future study.

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☆☆ All authors have seen and approved the manuscript.

Abbreviations: NIV, noninvasive ventilation; SMA1, Spinal Muscular Atrophy type 1.

https://doi.org/10.1016/j.sleep.2021.06.022

4. Suboptimal respiratory technology adherence

Introducing respiratory technology in the home setting may be overwhelming and burdensome to families without adequate patient and family-centered support. NIV adherence may be especially challenging given the child's conditioned anxiety with the hospital environment and healthcare providers in general. Anxiety may be further exacerbated by poorly fitting equipment, mask leaking, and the repeated association of discomfort and physiological arousal from struggling with therapy [9,10]. Additionally, respiratory therapies are time-consuming and prone to technical issues including overnight alarms resulting in poor sleep quality and quantity of the child as well as the family caregivers. This constellation of factors may all negatively impact adherence to respiratory technologies.

To date, there is limited pragmatic data demonstrating the impact of suboptimal adherence with supportive therapies on disease-modifying therapy efficacy. Further effort to promote adherence in these medically complex populations is paramount.

5. Opportunities to promote respiratory therapy acceptance and adherence

Caregivers of children with SMA1 undergo intense stress that is further complicated with major decision-making regarding goals of care and therapy plans for their child [11,12]. The early multidisciplinary team discussion of burdensome treatment programs and need for respiratory technology helps to establish treatment expectations and commitment from the outset [13]. Reframing prognostic uncertainty as an opportunity may empower patients and their caregivers, thereby helping them to regain some feelings of control over an overwhelming situation [14].

Adherence is fundamental to the success of all treatment plans and requires a therapeutic partnership between the medical team, family, and child. Despite the burden associated with respiratory therapies, NIV is increasingly used for infants in the home setting and is possible with ongoing open conversations about barriers to adherence [15,16]. Should there be poor tolerance to respiratory therapy, it is imperative for the multidisciplinary team to work together with the family in a positive and supportive manner to address all identified barriers [17]. A strengths-based approach for improved adherence in chronic illness includes ongoing engagement with social work, homecare nursing, and child life visits. Behaviour therapy techniques including positive reinforcement, graduated exposure, and counter conditioning may be helpful in improving NIV adherence in children [10]. Additionally, troubleshooting technological device issues can be facilitated through intensive support with a dedicated interprofessional team of nurses, physicians and respiratory therapists [17]. Real-time technology that connects families with an interprofessional long-term ventilation team may further augment this critical period of technology adjustment [18]. Lastly, brief but intensive inpatient admissions for NIV initiation, acclimatization and education can help to support NIV use in the home setting [19].

6. Conclusion

We are currently at an inflection point in history for the care of children with SMA1. Novel therapies are rapidly increasing in availability and newborn screening for SMA is becoming widespread. The importance of supportive therapies cannot be overstated to complement the effects of critical life-prolonging advances. We must reflect on the foundational aspects of medicine including essential supportive therapies and patient adherence while looking forward to future novel therapies on the horizon.

Funding

No grants or financial support were received for the preparation of this manuscript.

Acknowledgements

We would like to thank Jessica Sousa-Batista, caregiver of a patient benefiting from disease-modifying therapy, for providing thoughtful insight and feedback on this manuscript.

Conflict of interest

None declared.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: https://doi.org/10.1016/j.sleep.2021.06.022.

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10 June 2021
Available online 25 June 2021