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Respiratory Complications and Management in Duchenne Muscular Dystrophy and Amyotrophic Lateral Sclerosis

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Abstract

Introduction:

Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS) are rare recessive genetic disorders. Both conditions lead to a range of systemic complications, including those affecting the respiratory system. Respiratory and cardiovascular complications are identified as the most common causes of mortality in individuals with DMD and ALS. Early diagnosis of reduced respiratory parameters can delay the progression of respiratory system involvement. Available therapies, including gene therapy, pharmacological approaches, and conservative methods, can slow disease progression and prevent respiratory complications.

Aim of the study:

The aim of this study was to analyze the available treatment methods for Duchenne muscular dystrophy (DMD) and amyotrophic lateral sclerosis (ALS), with a particular focus on respiratory complications.

Materials and Methods:

A non-systematic review of scientific articles was conducted using the keywords “spinal muscular atrophy,” “Duchenne muscular dystrophy,” and “respiratory.” The review was performed in the PubMed and Google Scholar databases, analyzing a total of 31 sources published between 2008 and 2024.

Conclusions:

Early diagnosis of DMD or ALS is crucial for extending life expectancy and delaying the onset of adverse complications, including those affecting the skeletal, cardiovascular, and respiratory

systems. Currently, a broad range of therapeutic options is available to alleviate the daily challenges faced by patients and their families. Preventive measures and prompt responses to complications are essential to halt and delay further disease progression.

KEY WORDS: spinal muscular atrophy, duchenne muscular dystrophy, respiratory

INTRODUCTION

Duchenne muscular dystrophy (DMD) is a rare, genetically inherited disorder that predominantly affects males. The Duchenne muscular dystrophy gene is located on the short arm of the X chromosome. The mutation is inherited in an X-linked recessive pattern and is transmitted by carrier mothers. The incidence of the disorder is estimated at 1 in 3,500 male births. Dystrophin, a structural protein of muscle cells that connects the cytoskeleton to a glycoprotein complex in the cell membrane, prevents the disintegration of this complex. This stabilization influences membrane permeability. A deficiency or absence of dystrophin indicates the presence of Duchenne muscular dystrophy. [1] The disease leads to progressive muscle fiber weakness and degeneration. [11]

The first symptoms typically appear between the ages of 3 and 6 years. During this time, mobility issues and muscle weakness—primarily in the lower limbs—become apparent, as the hip muscles are the first to be affected. Around the age of 3, pseudohypertrophy of the calves develops. The gait becomes waddling, and patients experience difficulty climbing stairs. Muscle weakness is compensated by an abnormal posture, leading to lumbar lordosis and pelvic tilt. Achilles tendon contractures and weakened tibialis anterior muscles cause foot inversion or varus deformity. Children with DMD exhibit a positive Gowers' sign—using their hands and arms to "climb up" their body while attempting to stand. Over time, difficulties in maintaining head control become evident, with the head falling backward when sitting up due to weakened neck muscles. Nearly all children with DMD develop pathological scoliosis, which can cause additional difficulties with sitting and may negatively impact self-acceptance due to altered body image. [12,13] Delays in speech and intellectual development are also observed. [2]

By approximately 5 years of age, shoulder girdle muscles weaken. Between the ages of 10 and 14, children become immobilized as contractures and deformities develop. Over time, cardiac and pulmonary function deteriorates.

Spinal muscular atrophy (SMA) is also a genetic disorder, inherited in an autosomal recessive manner. Mutations in the SMN1 or SMN2 genes result in a deficiency of the SMN protein, which is essential for regulating gene expression in motor neurons. The lack of this protein leads to degeneration and apoptosis of anterior horn cells in the spinal cord and brainstem nuclei, ultimately causing muscle atrophy. SMA affects 1 in 6,000 to 1 in 10,000 individuals, making it the most common genetic cause of infant mortality. [16]

There are four clinical types of SMA:

- **Type I** – The most severe form, with the first symptoms appearing before 6 months of age. Infants never achieve early developmental milestones, such as sitting, and typically die before the age of 2 due to respiratory complications.
- **Type II** – An intermediate form, with symptoms manifesting between 7 and 18 months of age. Infants are able to sit but cannot stand independently.
- **Type III** – A mild form in which patients can sit, walk, and usually live into adulthood.
- **Type IV** – Occurs in adulthood and is the mildest form of the disease. [4]

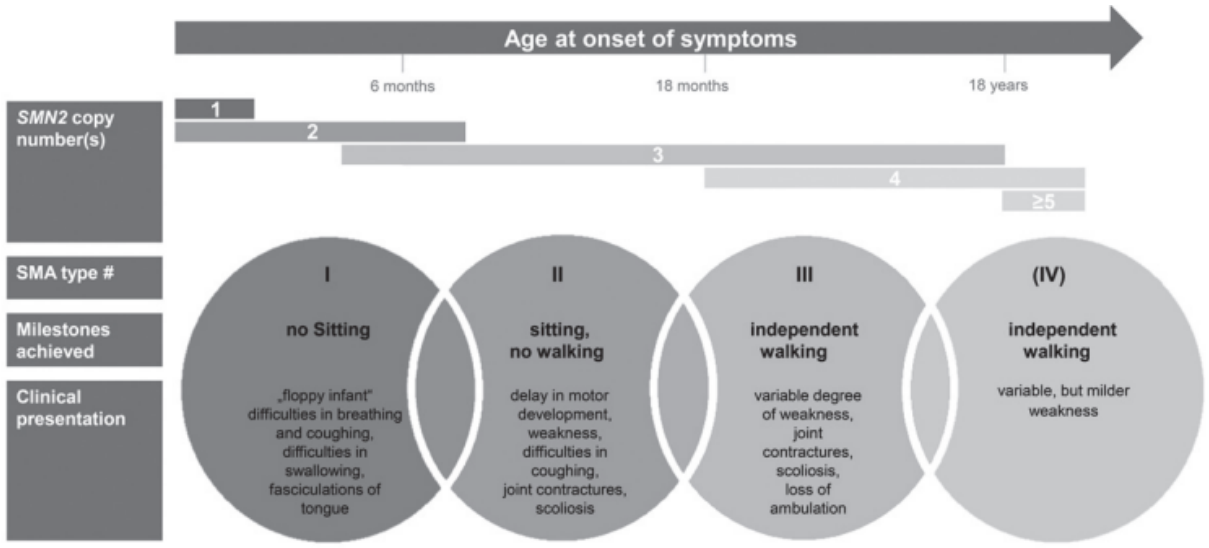

Fig. 1. The clinical classification of SMA subtypes, based on the onset of the disease, achieved developmental milestones, symptoms, and the number of SMN2 gene copies. [27]

DIAGNOSIS

The diagnostic process for Duchenne muscular dystrophy (DMD) begins with patient observation and a detailed family history. Initially, it is essential to measure serum levels of aminotransferases and creatine kinase. Subsequently, genetic testing is performed. If genetic testing yields negative results, a muscle biopsy is conducted to evaluate the presence of dystrophin. Measuring creatine kinase levels helps differentiate DMD from neurogenic disorders, such as spinal muscular atrophy (SMA).

Electromyography (EMG) is also valuable in diagnosing DMD, as it determines whether the dysfunction originates from the muscle itself or its innervation, indicating whether the pattern is myogenic or neurogenic. However, EMG does not specify the type of dystrophy.
For patients with DMD, echocardiography, electrocardiography (ECG), and spirometry are recommended every two years until the age of 10. Afterward, the frequency of these follow-up tests should increase. [2]

In spinal muscular atrophy (SMA), diagnosis relies primarily on genetic testing, specifically quantitative assessment to determine the number of SMN1 and SMN2 gene copies. If a single SMN1 copy is preserved in a patient with suspected SMA, further testing for point mutations is recommended. However, the absence of such mutations does not rule out SMN1-dependent SMA. [8]

MANAGEMENT

The primary goal of treating patients with Duchenne muscular dystrophy (DMD) is initially to improve and subsequently maintain their functional status while prolonging the period of independence. Additionally, minimizing complications related to the musculoskeletal system, such as reducing the risk of scoliosis and preventing cardiomyopathy, is essential. Strengthening skeletal muscles and minimizing spinal curvature positively impact respiratory function. [5]

At the early stages of the disease, the inclusion of glucocorticosteroids in therapy is crucial [2], although their mechanism of action in DMD is not fully understood. The most commonly studied agents are prednisone and deflazacort. Prednisone has been shown to increase the number of regenerating muscle fibers in boys with DMD, reduce dendritic cells and fibroblasts, and increase the number of satellite cells. [5]

Patients are also administered preparations containing vitamin B and mono- and triphosphate compounds that influence muscle metabolism. A controversial treatment method involves the transplantation of myoblasts from the patient's father into the child's muscles. [6] In 2014, a drug named Translarna was developed. However, it is only suitable for children with the so-called nonsense mutation who are still able to walk independently. This drug enables the production of dystrophin of normal length, thereby halting disease progression. [3]

Currently, three approved drugs are available for the treatment of spinal muscular atrophy (SMA): Spinraza (nusinersen), Zolgensma (onasemnogene abeparvovec), and Evrysdi (risdiplam). Causal treatment strategies are categorized into:

- Increasing the efficiency of the SMN2 gene in producing the SMN protein.
- Introducing the exogenous SMN1 gene into the body through gene therapy methods.

Nusinersen is the only one of the three drugs approved for treating patients regardless of the clinical type of SMA. These disease-modifying therapies increase SMN protein levels in peripheral neurons of the corticospinal tract, preventing their degeneration. [9]

Physical therapy for patients with Duchenne muscular dystrophy (DMD) aims to slow the progression of the disease. Muscle training should be conducted cautiously, with exercise stopping at the first signs of fatigue. Active free exercises, coordination, and balance exercises are implemented. The focus should primarily be on strengthening the endurance of the shoulder and hip girdle muscles. The PNF (Proprioceptive Neuromuscular Facilitation) technique is also applied for DMD patients. Additionally, respiratory exercises and patient verticalization are important, especially when independent mobility ceases. Preventing or addressing contractures, if they have already developed, is essential. In the final stage of the disease, non-invasive ventilation can be used. [7]

Preliminary data concerning adults with SMA, as well as research conducted on animal models, suggest that physical exercise offers potential benefits. Studies have observed a trend toward improved muscle strength and motor function. Neuromuscular electrical stimulation can enhance the oxidative capacity of skeletal muscles in cases of atrophy, while functional electrical stimulation may positively affect weak muscles. [10]

In spinal muscular atrophy, there is a significant risk of scoliosis development. Therefore, the use of braces may be helpful, although they do not stop scoliosis progression but rather assist in maintaining proper posture. [8]

RESPIRATORY COMPLICATIONS

The most common respiratory difficulties in these conditions include sleep-related breathing issues (e.g., sleep apnea), problems with expectorating secretions, and increased susceptibility to lung infections. As the disease progresses, a key parameter, forced vital capacity (FVC), also declines. A decrease in FVC by more than 20% when the patient transitions from a sitting to a lying position is a specific indicator of diaphragm weakness and an important prognostic factor in the disease progression. [14]

A decline in FVC, FEV1, and peak expiratory flow (PEF) values is noticeable from childhood, although certain parameters, such as tidal volume (TV), minute ventilation (MV), and respiratory rate (RR), show a significant decrease compared to physiological levels. TV significantly declines around the age of 17, MV around the age of 18, and RR noticeably drops after the age of 22. [20]

MANAGEMENT OF RESPIRATORY COMPLICATIONS

Studies suggest that non-invasive ventilation (NIV) can delay the deterioration of lung function. However, combining it with corticosteroid therapy may accelerate this process. [17] Typically, patients with Duchenne muscular dystrophy (DMD) die due to cardiovascular-respiratory failure before the age of 20. [3] The possibility of surviving until around 30 years of age is associated with mechanical ventilation and corticosteroid use. [15]

Corticosteroids can significantly improve the respiratory parameters of patients with DMD. It is suggested that they should be introduced into therapy before the age of 10. Their use has been observed to markedly slow the decline in FVC values—by nearly 10 times—compared to patients who do not receive corticosteroids. [21]

The most commonly chosen method of NIV is nocturnal ventilation. However, studies emphasize the need for long-term 24-hour NIV. This may help avoid tracheostomy, and patients who cannot be weaned off the ventilator may use NIV combined with mechanical cough assistance. This method is considered safer than using a tracheostomy. [22,23] The same applies to patients with SMA. NIV can be successfully used for these patients, and if intubation is necessary due to acute respiratory failure, NIV with mechanical cough assistance can be used after extubation. [24]

Delaying the initiation of lung ventilation support in patients with SMA can lead to atelectasis and other complications, such as upper respiratory tract infections. However,

monitoring breathing during sleep cannot be a reliable predictor for the need for NIV in SMA patients. [25]

The accumulation of free radicals and oxidative stress have been identified as factors that accelerate the progression of Duchenne muscular dystrophy (DMD). In individuals with DMD, elevated levels of lipid peroxidation products and protein oxidation are observed. Antioxidant therapy may help inhibit lipid peroxidation, consequently stimulating mitochondrial electron flow and cellular energy production, thus improving respiratory muscle efficiency and respiratory function. The use of antioxidants like idebenone is supported by the lower number of side effects compared to corticosteroid use. However, in studies, idebenone has not shown improvements in quality of life for patients and has only a minor or no effect on increasing muscle strength. It has been noted, however, to have a positive impact on slowing the decline in vital capacity and the ability to expel air from the lungs and airways. [18,19]

It is also important to highlight the potential role of modern technologies in the treatment of muscular dystrophies. Preclinical studies have consistently shown that CRISPR/Cas9 can effectively correct dystrophin mutations in animal models of DMD. CRISPR/Cas9 is a revolutionary gene-editing tool that allows for precise modifications by utilizing natural DNA repair mechanisms. The system uses guide RNA (gRNA) to direct the Cas9 enzyme to a specific DNA sequence, where the enzyme introduces a double-strand break (DSB). [26]

Fig. 2.

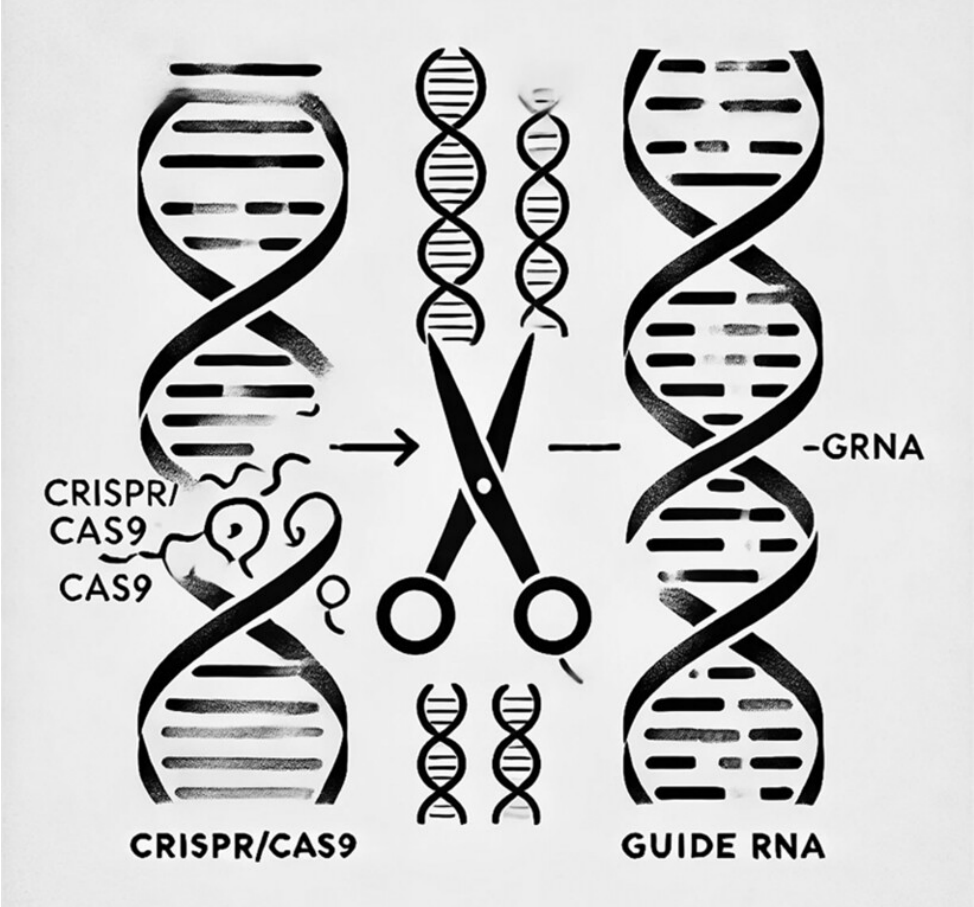

Illustration of basic mechanism of CRISPR/Ca9 gene editing. [26]

One of the main challenges in using CRISPR/Cas9 therapy for Duchenne muscular dystrophy (DMD) is the effective delivery of gene-editing components to muscle cells, due to the large size of the dystrophin gene. Another significant challenge is ensuring the long-term safety of CRISPR/Cas9-based therapies. Unintended editing of other parts of the genome, aside from the intended target, may occur in CRISPR/Cas9 therapy. This could have serious consequences, including oncogenic potential. [26]

Salbutamol has shown a positive effect in patients with spinal muscular atrophy (SMA) – studies have demonstrated an increase in muscle strength, forced vital capacity, and lean body mass, as well as improvement in motor functions. [28] One of the possible mechanisms of action of salbutamol in SMA patients is the promotion of SMN2 transcription and exon 7 splicing of SMN2 in fibroblasts, which leads to an increase in intracellular SMN protein levels. [29]

Harahap et al. proposed an alternative mechanism of action for salbutamol. Salbutamol may

inhibit ubiquitin-dependent protein degradation, leading to an increase in SMN protein levels. [30]

VACCINATION

In Poland, there are currently no available data on the use of gene therapy for spinal muscular atrophy (SMA) alongside steroid administration in children who have received live tuberculosis vaccines (BCG). In the United States, it is recommended to adjust the patient's vaccination schedule to account for the simultaneous administration of corticosteroids before and after the infusion of onasemnogen abeparvovec (Zolgensma®). However, BCG vaccination is not administered as a mandatory vaccine in the U.S. The BCG vaccine is the only live vaccine that is commonly given to newborns, even before genetic test results are available. Due to this fact, administering a live vaccine to children who are identified as positive in screening programs may pose a significant risk. Polish guidelines regarding the use of the BCG vaccine include a protocol before and after gene therapy. If the patient has already received gene therapy, the administration of the BCG vaccine should be postponed for at least 30 days after completing immunosuppressive corticosteroid treatment. If the patient has not yet received gene therapy, the schedule is presented in Figure 3.

Fig. 3. he proposed vaccination schedule for patients during the screening diagnostic process. [31]

Inactivated vaccines do not pose a risk for patients undergoing immunosuppressive treatment, and therefore, the vaccination schedule does not require modification. It is recommended that infants with SMA receive vaccinations with an acellular pertussis antigen, preferably in combination, e.g., 6-in-1 or 5-in-1 vaccines. [31]

CONCLUSIONS

Both Duchenne muscular dystrophy (DMD) and spinal muscular atrophy (SMA) require significant involvement and determination from the patients themselves, as well as their families, physicians, physiotherapists, nurses, and all others in their surroundings. Early diagnosis of the patient seems essential. Although symptoms can be non-specific, the physician should also consider the possibility of serious diseases such as DMD or SMA in their still undiagnosed patients. In addition to pharmacotherapy, physiotherapy plays a crucial role in preventing muscle contractures, strengthening specific muscle groups, improving joint range of motion, preventing postural deformities (scoliosis), and respiratory infections. Psychological care for patients diagnosed with DMD or SMA, as well as their families, who are equally affected by the condition, should not be overlooked. It is important to note that diseases like DMD or SMA and their consequences do not affect only the individual but the entire surrounding environment, which must adapt to the condition. Patients face mobility issues, which complicates access to school, making the role of educators who implement individualized teaching programs crucial. In terms of treatment, it appears necessary to establish a well-coordinated team of specialists. Science shows that no decision regarding the patient's therapy should be made individually by one specialist, as Duchenne muscular dystrophy and spinal muscular atrophy are far more complex issues than those limited to one specialty. Currently, we have a wide range of possibilities to prevent complications and provide treatment for patients with DMD and SMA in a way that ensures their normal functioning in everyday life.

DISCLOSURE

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Software: Magdalena Rosa- Bończak, Klaudia Anna Pawełek

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References

1. Piusińska K, Węgrzynowska EJ. *Medical and social aspect of Duchenne muscular dystrophy as a chronic disease in a 14-year-old child.* Pielęgniarstwo w Opiece Długoterminowej / Long-Term Care Nursing. 2019;4(3):42-49. doi:10.19251/pwod/2019.3(5).

2. Puza K, Trociuk E, Dolińska C, Snarska KK, Lewko J, Olejnik B. *Dystrofia Duchenne'a - opieka i pielęgnacja chorego w kolejnych etapach choroby.* Sytuacje trudne w ochronie zdrowia. T. 2. Praca zbiorowa. Red. Agnieszka Lankau, Dorota Kondzior, Elżbieta Krajewska-Kułak.Białystok: Uniwersytet Medyczny w Białymstoku, 2017, s. 165-175.

3. Majewicz P, *Wybrane obszary wspomagania rozwoju dzieci i młodzieży z dystrofią mięśniową*. Państwo i Społeczeństwo. 2020 (XX) nr 1. DOI: 10.34697/2451-0858-pis-2020-1-003

4. Szczerba A, Śliwa A, Żarowski M, Jankowska A. *Molekularne podłoże i terapia rdzeniowego zaniku mięśni.* Neurologia Dziecięca 2018; 27, 55: 39-46. DOI:10.20966/chn.2018.55.429

5. Kostera- Pruszczyk A. *Glikokortykoidy w leczeniu dystrofii mięśniowej Duchenne'a – standard postępowania.* Neurologia Dziecięca 2011; 20, 40: 11-14

6. Sochoń K, Zalewska A, Kur M, Wojtkowski J, Kułak W. *Fizjoterapia w dystrofii mięśniowej typu Duchenne'a.* Współczesne metody rehabilitacji dzieci i młodzieży. Białystok: Uniwersytet Medyczny w Białymstoku, 2014, s. 80-90.

7. Kijowski S. *Fizjoterapia jako alternatywa w postępującej dystrofii mięśniowej.* Przegląd Medyczny Uniwersytetu Rzeszowskiego i Narodowego Instytutu Leków w Warszawie, Rzeszów 2012, 3, 379–285

8. Jędrzejowska M, Kostera- Pruszczyk A. *Rdzeniowy zanik mięśni – nowe terapie, nowe wyzwania.* Neurologia Dziecięca 2017; 26, 52: 11-17. DOI:10.20966/chn.2017.52.400

9. Bodzioch M. *Postępy w leczeniu rdzeniowego zaniku mięśni.* Polski Instytut Evidence Based Medicine, Zakład Genetyki Synevo Sp. z o.o. Medycyna Praktyczna Neurologia; 2021/01

10. Iłżecka J. *Rehabilitacja w rdzeniowym zaniku mięśni.* Med Og Nauk Zdr. 2021;27(3):277-280. doi:10.26444/monz/137080.

11. Bulut N, Yardimci BN, Ayvat E, Aran OT, Yilmaz Ö, Karaduman A. The effect of two different aerobic training modalities in a child with spinal muscular atrophy type II: a case report. J Exerc Rehabil. 2019;15(2):322-326. Published 2019 Apr 26. doi:10.12965/jer.1836604.302

12. Venugopal V, Pavlakis S. Duchenne Muscular Dystrophy. [Updated 2023 Jul 10]. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing; 2024 Jan-. Available from: https://www.ncbi.nlm.nih.gov/books/NBK482346/

13. Garg S. Management of scoliosis in patients with Duchenne muscular dystrophy and spinal muscular atrophy: A literature review. *J Pediatr Rehabil Med*. 2016;9(1):23-29. doi:10.3233/PRM-160358.

14. LoMauro, Antonella et al. “Assessment and management of respiratory function in patients with Duchenne muscular dystrophy: current and emerging options.” *Therapeutics and clinical risk management* vol. 11 1475-88. 28 Sep. 2015, doi:10.2147/TCRM.S55889

15. Mavrogeni S, Markousis-Mavrogenis G, Papavasiliou A, Kolovou G. Cardiac involvement in Duchenne and Becker muscular dystrophy. *World J Cardiol*. 2015;7(7):410-414. doi:10.4330/wjc.v7.i7.410

16. Ross, Lainie Friedman, and Jennifer M Kwon. “Spinal Muscular Atrophy: Past, Present, and Future.” *NeoReviews* vol. 20,8 (2019): e437-e451. doi:10.1542/neo.20-8-e437

17. Angliss ME, Sclip KD, Gauld L. Early NIV is associated with accelerated lung function decline in Duchenne muscular dystrophy treated with glucocorticosteroids. BMJ Open Respir Res. 2020;7(1):e000517. doi:10.1136/bmjresp-2019-000517

18. Garegnani L, Hyland M, Roson Rodriguez P, Escobar Liquitay CME, Franco JV. Antioxidants to prevent respiratory decline in people with Duchenne muscular dystrophy and progressive respiratory decline. Cochrane Database Syst Rev. 2021;11(11):CD013720. Published 2021 Nov 8. doi:10.1002/14651858.CD013720.pub2

19. Garegnani L, Hyland M, Roson Rodriguez P, Escobar Liquitay CME, Franco JV. Antioxidants to prevent respiratory decline in people with Duchenne muscular dystrophy and progressive respiratory decline. *Cochrane Database Syst Rev*. 2021;11(11):CD013720. Published 2021 Nov 8. doi:10.1002/14651858.CD013720.pub2

20. "Evolution of respiratory function in Duchenne muscular dystrophy from childhood to adulthood." Antonella LoMauro, Marianna Romei, Sandra Gandossini, Riccardo Pascuzzo, Simone Vantini, Maria Grazia D'Angelo and Andrea Aliverti. *Eur Respir J* 2018; 51: 1701418. *Eur Respir J*. 2018;51(4):1751418. Published 2018 Apr 4. doi:10.1183/13993003.51418-2017

21. McDonald CM, Gordish-Dressman H, Henricson EK, et al. Longitudinal pulmonary function testing outcome measures in Duchenne muscular dystrophy: Long-term natural history with and without glucocorticoids. *Neuromuscul Disord*. 2018;28(11):897-909. doi:10.1016/j.nmd.2018.07.004

22. Bach JR, Martinez D. Duchenne muscular dystrophy: continuous noninvasive ventilatory support prolongs survival. *Respir Care*. 2011;56(6):744-750. doi:10.4187/respcare.00831

23. McKim DA, Griller N, LeBlanc C, Woolnough A, King J. Twenty-four hour noninvasive ventilation in Duchenne muscular dystrophy: a safe alternative to tracheostomy. *Can Respir J*. 2013;20(1):e5-e9. doi:10.1155/2013/406163

24. Al-Subu AM, Adams CK, Dykstra SA, et al. Management of Critically Ill Patients With Spinal Muscular Atrophy Admitted With Acute Respiratory Failure. *Respir Care*. Published online January 3, 2023. doi:10.4187/respcare.10353

25. Menard J, Seferian AM, Fleurence E, et al. Respiratory management of spinal muscular atrophy type 1 patients treated with Nusinersen. *Pediatr Pulmonol*. 2022;57(6):1505-1512. doi:10.1002/ppul.25899

26. Ali A, Rahman MY, Sheikh D. The Role of CRISPR/Cas9 in Revolutionizing Duchenne's Muscular Dystrophy Treatment: Opportunities and Obstacles. *Glob Med Genet*. 2024;11(4):349-357. Published 2024 Oct 18. doi:10.1055/s-0044-1791803

27. Schorling DC, Pechmann A, Kirschner J. Advances in Treatment of Spinal Muscular Atrophy - New Phenotypes, New Challenges, New Implications for Care. J Neuromuscul Dis. 2020;7(1):1-13. doi:10.3233/JND-190424

28. Nishio H, Niba ETE, Saito T, Okamoto K, Takeshima Y, Awano H. Spinal Muscular Atrophy: The Past, Present, and Future of Diagnosis and Treatment. *Int J Mol Sci*. 2023;24(15):11939. Published 2023 Jul 26. doi:10.3390/ijms241511939

29. Angelozzi C, Borgo F, Tiziano FD, Martella A, Neri G, Brahe C. Salbutamol increases SMN mRNA and protein levels in spinal muscular atrophy cells. *J Med Genet*. 2008;45(1):29-31. doi:10.1136/jmg.2007.051177

30. Harahap NIF, Nurputra DK, Ar Rochmah M, et al. Salbutamol inhibits ubiquitin-mediated survival motor neuron protein degradation in spinal muscular atrophy

cells. *Biochem Biophys Rep*. 2015;4:351-356. Published 2015 Oct 28. doi:10.1016/j.bbrep.2015.10.012

31. Kotulska K, Jozwiak S, Jedrzejowska M, et al. Newborn screening and gene therapy in SMA: Challenges related to vaccinations. *Front Neurol*. 2022;13:890860. Published 2022 Nov 23. doi:10.3389/fneur.2022.890860