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Spinal Muscular Atrophy Cases and Therapeutic Pathways in Cities in Western Libya

Mabrooukah Ishrayhah[1,*], Areej Dabooub[2], Ebtesam Beshna[3], Ayat kamal Salem[1], Sara Nouralddeen[1], Fatima AL taher Ali[1]

[1]Department of pharmacology and toxicology, Faculty of Pharmacy, University of Zawia, Libya.
[2]Department of pharmacognosy, Faculty of Pharmacy, University of Zawia, Libya.
[3]Department of pharmaceutics and industrial pharmacy , Faculty of Pharmacy, University of Zawia, Libya.

*Corresponding author's E-mail: m.isharyhah@zu.edu.ly

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Abstract

Autosomal recessive mutations in the survival motor neuron1 (SMN1) gene cause spinal muscular atrophy (SMA), which is characterized by increasing muscle weakening and motor neuron loss. It is important to diagnose the disease and start treatment procedures early to achieve the best possible outcome. In this study, we will shed light on this disease and the most important therapeutic pathways that have been taken to stop or slow its progression and improve the patient's quality of life, with restriction the cases in western region cities of Libya. Identical questionnaire, made up of 15 questions. The data then was evaluated by Microsoft Excel software for analysis. As a result of this study, with regard to region, gender, and type of atrophy, male atrophy patients - in the Al-zawia region - with types I and III have the highest rate among all data, As for gender, the matter is similar to what we saw in another study entitled (Gender difference in patients with SMA - Are males more susceptible to infection), where the number of males was greater than females. According to our research, the western part of Libya has a low rate of adoption of novel and creative treatments for the treatment of illness. (less than 50% using risdiplam and nusinersin). In conclusion this study shows that spinal muscular atrophy affects males more than females and that physical therapy alleviates in most cases the postural symptoms that affect patients due to atrophy and weakness of the muscles resulting from their inactivity. As for the small group that took the medicine before its arrival, it is likely that they obtained it outside the country. Most patients suffer from difficulty breathing, spinal problems, and psychological problems, which increases the need for multidisciplinary care.

Keywords

Spinal muscular atrophy, neuromuscular disease, physiotherapy.

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INTRODUCTION

Spinal Muscular Atrophy (SMA) is a genetic neuromuscular disorder characterized by the degeneration of motor neurons, leading to muscle weakness and atrophy. It is primarily caused by mutations in the survival motor neuron 1(SMN1) gene, resulting in insufficient levels of the SMN protein, crucial for motor neuron survival.

Autosomal recessive mutations in the survival motor neuron1 gene cause spinal muscular atrophy (SMA), which is characterized by increasing muscle weakening and motor neuron loss.[1] Only motor function is disrupted, while sensory neurons remain untouched, as only α motor neurons are gradually destroyed. As the condition worsens, this loss of function causes the proximal voluntary muscles of the arms, legs, and occasionally the trunk to weaken and gradually atrophy symmetrically.[1] Legs are more impacted than arms, arms are more affected than the face and diaphragm, and proximal muscles are more engaged than distal muscles.[2]

Its overall incidence is estimated at 1/10,000 live births, and despite being included in the group of rare diseases, it causes an important family, social, and economic impact;[3,4] as it is one of the most common autosomal recessive hereditary disorders, and it is the monogenic disease with higher infant mortality.[3,4]

Patients with SMA-5q have insufficient SMN protein (survival motor neuron protein), whose functions influence the axonal transport of molecules, mitochondrial metabolism, and ribonucleic acid (RNA) processing in neurons. The SMN protein is encoded by 2 genes, SMN1 and its homologous gene, SMN2, located on chromosome 5.[5,6]

The SMN protein is made by two genes, the SMN1 and SMN2 genes. Most patients with SMA lack the SMN1 gene but have the SMN2 gene, which mostly produces a 'short' SMN protein which cannot work properly on its own.[7] With an incidence estimated to be between 1:6,000 and 1:10,000 and it, is one of the most prevalent pediatric recessive genetic diseases.[8] Males are more likely than females to have it.[9,10] The degeneration of anterior horn cells in the spinal cord, which results in gradual proximal weakness with variable degrees of muscular atrophy, is the disease's defining feature.[11]

The impact of SMA on individuals is also evolving due to the availability of disease-modifying therapies.[12] For instance, early treatment may help a child with SMA Type 1 meet milestones like sitting or standing on their own that are usually attained by children with SMA Type 2 or Type 3.12 Without therapy, children with Type 2 or Type 3 SMA may also lose the capacity to sustain their accomplishments. The approved treatments of today can have an impact on results, particularly if administered early. Each child reacts differently to treatment, and a child's potential milestones are determined by how SMA impacts them prior to treatment.[12]

Nusinersen (SpinrazaTM) was approved by the European Medicines Agency (EMA) in June 2017 and the U.S. Food and Drug Administration (FDA) in December 2016 as the first medication to treat SMA in adults and children of all kinds.[13,14] By boosting exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts, this treatment modifies the SMN2 gene and increases its production of protein,[15] which is essential for the upkeep of motor neurons.[13]

Repeated intrathecal injections of nusinersen are necessary and frequently result in thrombocytopenia and injection-site side effects.[16] Additionally, the abnormal curvature of the spine, known as scoliosis, can frequently make it difficult to inject nusinersen intrathecally.[17] Research indicates that approximately 40% of users benefit from it by becoming stronger and delaying the progression of their illness.[15]

The FDA on august 7, 2020 approved the orally-administered drug risdiplam (Evrysdi) to treat patients age two months of age and older with SMA.[16] Age and body weight determine the permissible dosage of risdiplam.[18] In order to make more functional SMN protein and enable the protein to reach the nerve cells when required, this medication targets the backup copy of the SMN2 gene and increases exon 7 inclusion in SMN2 messenger ribonucleic acid (mRNA) transcripts via small molecules.[19] They target not just the central nervous system but also the peripheral nervous system, as well as nonneuronal organs and tissues, because they are accessible upon oral administration and transported systemically.[15,20,21,22] A possible drawback of tiny splice modifiers is their increased likelihood of off-target effects when compared to medications based on antisense oligonucleotides (ASOs).[23] There were no documented severe side effects from the medication.[24] On May 24, 2019, the FDA authorized onasemnogene abeparovec-xioi (Zolgensma ™) gene therapy for infantile-onset SMA in children under two.[13] For the treatment of spinal muscular atrophy (SMA), olesoxime (TRO19622), a new neuroprotective substance that targets the mitochondria, is undergoing a crucial clinical effectiveness investigation.[25]

In this study, we will shed light on this disease and the most important therapeutic pathways that have been taken to stop or slow its progression and improve the patient's quality of life, with restriction the cases in western region cities of Libya.

MATERIALS AND METHODS

Identical questionnaire, made up of 15 questions were used. The questions were set to find out the number of patients in the western region who suffer from spinal atrophy, and they were also asked about their ability to obtain effective medicines to stop the progression of this disease. Also they were also asked about secondary auxiliary medicines and other procedures that they followed in the event that they were unable to obtain effective medicines. They were asked about the most important health problems and complications that they suffer from due to this disease. From January 2023 to April 2023, a cross-sectional survey study was conducted among patients in western region of Libya. A snowball sampling method was used. A validated, self-administered questionnaire was used to collect basic sociodemographic data from the participants, as well as information regarding, diagnostic method of disease, parents relationship, medications used and knowledge of their complication. A validated, self-administered questionnaire was used to collect data. It also divided into two sections. The initial part of the questionnaire focused on assessing the participants' sociodemographic characteristics including gender, age, and occupation. The second part aimed to explore the participants' relationship between parents' medication, physical therapy and medication. Every participant directly received a questionnaire. Additionally, the participants were assured that all collected information would be treated anonymously and maintained confidentially. The participants were explicitly informed of their right to discontinue participation at any time without the obligation to provide

a reason. To evaluate the responses of the study sample, Microsoft excel sheet were used to analyze the data. the survey's data are displayed as percentages (%). Results for categorical variables were displayed either graphically or as percentage-based values.

RESULTS

The total number of responses received was 22, and these responses were from different cities in the west of Libya. During 4 months' study 2023. The data then was evaluated by Microsoft Excel software for analysis.

Firstly, Spinal muscular atrophy patients on relation to their cities were nine patients from Al-zawia, while Two from Almayah, both Misrata and Tripoli were three, Sabratah and alajaylat and Surman were one patient (Figure1).

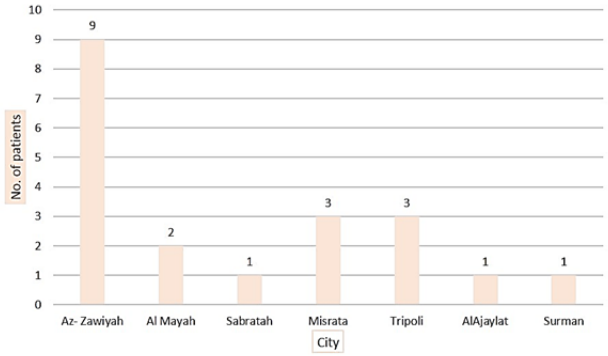

Figure 1. Patients' cities.

The largest percentage of patients in the western region was male, equivalent to 68%. On the other hand, the percentage of female patients was 32% (Figure 2).

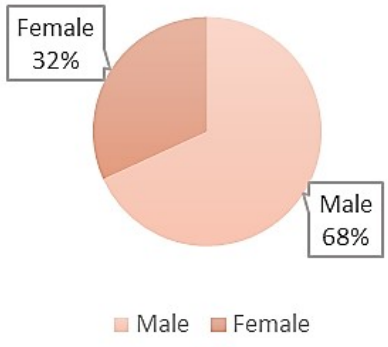

Figure 2. Patients' sex.

Figure 3 shows the ages of SMA patients in west Libya.

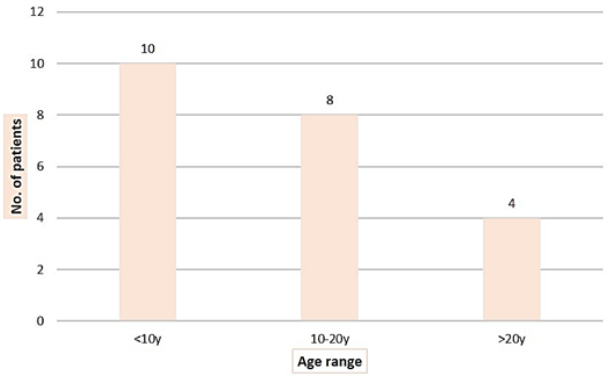

Figure 3. Ages bracket.

Then, based on the fourth question, in which we inquire about the age at which the symptoms of the disease appeared, we were able to deduce the type of spinal atrophy in each patient. We found that the percentage of patients with the first type is 42%, the second type is 8%, while the third type is 42%, and the fourth type is 8%.

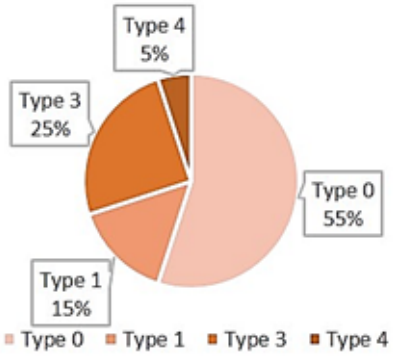

Figure 4. SMA types.

Table 1 highlights the different diagnostic methods used by spinal atrophy patients, as the disease was diagnosed in 18% of patients using an electromyogram, and in 18% of them using a muscle sample, while the largest percentage was for those who used a blood sample to diagnose their condition, estimated at 50%. The smaller percentage of those who used other methods is estimated at about 14%.

After that, the patients were asked whether there was a relationship between the parents, were 45% of patients answered affirmatively, and 55% of patients answered negatively (Table 2).

Table 1. Diagnostic method.

Diagnostic method	Number of patients	%
Blood sample	11	48%
EMG	4	18%
Muscle sample	4	17%
MRI	1	4%
Otherwise	3	13%

Table 2. Relationship between parents.

Relationship between the parents	Number of patients	%
Present	9	45%
Absent	11	55%

The eighth and ninth questions shed light on the medicines that the patients got, and we found that 38% of them did not get any medicine, while 14% take tonics, 14% take vitamins, 9% of them take analgesics. While 5% of the patients take Anti rheumatic drugs, 5% used Ventoline, and 5% used they take the antidepressant amitriptyline, and the rest take basic medications for atrophy (5% take Nusinersen and 5% take risdiplam) (Figure 5).

Then we added a question about the difficulty of finding medicine in pharmacies. We found that 71% of patients find it difficult to find medicine in pharmacies, and 29% of them obtained the medicine easily. Most of the patients, when asked about the cost of obtaining medication from pharmacies, answered that the cost of treatment was high, and they are 86% of the patients, while 14% of the patients stated that the cost was cheap (Figure 6).

Finally, based on the need of the majority of patients for physical therapy and their resort to it as a first solution to alleviate the muscle weakness that they suffer from in particular, we asked them whether they performed physical therapy and their opinions about its effectiveness in their condition. We found that 18% did not perform physical therapy, while 82% did it. who are they; 41% of them said it was effective, and 41% said it was not effective for their condition (Figure 7).

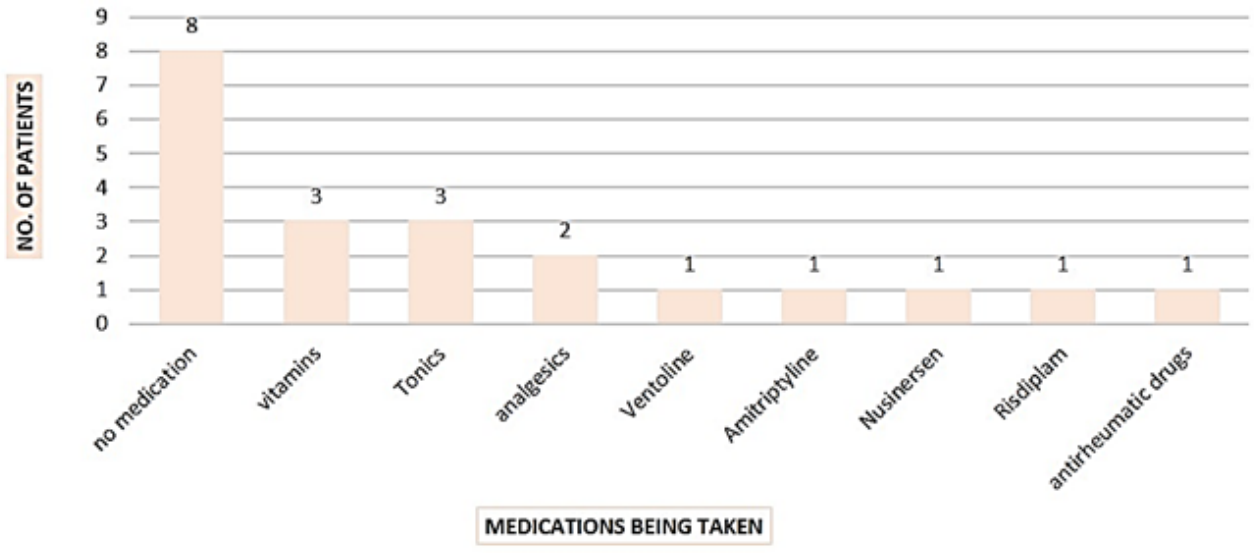

Figure 5. Medication being taken.

Figure 6. Ease of obtaining the SMA medicine in pharmacies.

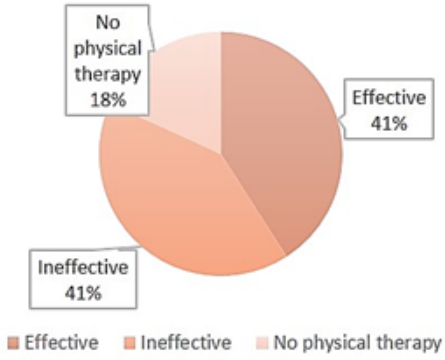

Figure 7. Physical therapy effectiveness.

DISCUSSION

When we presented the questionnaire to patients with atrophy in the western region of Libya, we faced some problems in filling out the questionnaire, which were as follows: the number of atrophy patients in the western region is not large, therefore we faced difficulty in obtaining a sufficient number of questionnaires to conduct this study, the patient's awareness of disease is still weak, so some patients did not respond to many questions. In addition, to the difficulty of obtaining the medicine, which limited obtaining sufficient information about its effectiveness. Our findings also indicate that the utilization rate of new and innovative therapies for disease management is low in the western region of Libya (less than 50% using risdiplam and nusinersin). Our finding with regard to the obstacles to the use of gene therapy, they were asked about the difficulty of obtaining the treatment in terms of its availability in pharmacies and its cost. On the other hand, the rest were satisfied with the use of palliative care that might they relieve a little of the symptoms, which are often available as a temporary alternative until they obtain the required medicine comparison with a study in Saudi Arabia that find the utilization rate of novel and innovative treatments for SMA management is low in Saudi Arabia[26] (more than 50% of the respondents reported never prescribing nusinersen to their patients). However, most SMA patients who were prescribed nusinersen are taking it. In contrast, nearly all of the respondents did not prescribe onasemnogene abeparvovec, and no patient was started on it because this drug is not yet approved by the Saudi FDA. Also two-thirds of the respondents said that only supportive care is available for their patients, and one-third used palliative care, do-not-resuscitate, and no endotracheal intubation, which is in accordance with international consensus guidelines.[27,28]

As a result of this study, with regard to region, gender, and type of atrophy, male atrophy patients - in the AL-Zawia region - with types I and III have the highest rate among all data, As for gender, the matter is similar to what we saw in another study entitled (Gender difference in patients with spinal muscular atrophy - Are males more susceptible to infection)[29] where the number of males was greater than females. Higher male/female ratio among SMA patients were correlated with higher SMA incidence and prevalence rates, and inversely correlated to the total population male/female ratio. This result suggests that genetic background may play a role in sex differences in SMA patients from different registry datasets.[30]

Sex differences have been demonstrated in brain physiology and behavior during development and adulthood, and sex is also a significant variable affecting the prevalence and incidence of some neurological disorder.[31,32,33]

It was noted in this study: that most patients suffer from a mixture of complications, including difficulty breathing, about 50%, which is one of the most severe complications of this disease, and in second place comes scoliosis, which affects patients at a rate of 14%, noting that both symptoms may be present together in some cases. Patients, in others, may be accompanied by constipation or back pain, but about 25% of them denied having any complications. Therefore, most of the patients required respiratory supportive care, with some using medications Calventolin, in addition to painkillers for bone pain and medicines for rheumatism, as one of the patients mentioned that he suffers from depression and is used for that Amytriptylin.

One of the things that we noticed in our study is that some patients mentioned in their notes that they cannot walk, which is expected as we have seen in other studies conducted in different Western countries, especially among patients with the first and second types.

Based on the fact that this disease is hereditary, we focused on the question about the kinship relationship between the parents, and we found that 45% of the patients denied the existence of a relationship between their parents, and 55% of them answered that there is no a relationship. Therefore, we cannot ignore the danger of consanguineous marriage in the event of genetic diseases in the history Family.

CONCLUSION

This study shows that spinal muscular atrophy affects males more than females and that physical therapy alleviates in most cases the postural symptoms that affect patients due to atrophy and weakness of the muscles resulting from their inactivity. In addition, most patients were unable to obtain risdiplam because the period during which this study was conducted was before the drug arrived in Libya.

REFERENCES

1. Wang CH, Finkel RS, Bertini ES, Schroth M, Simonds A, Wong B, et al. Consensus statement for standard of care in spinal muscular atrophy. J Child Neurol. 2007;22:1027-49.
2. Darras BT. Spinal muscular atrophies. Pediatr Clin North Am 2015;62:743–766. Doi: 10.1016/j.pcl.2015.03.010
3. Kolb SJ, Kissel JT. Spinal muscular atrophy: a timely review. Arch Neurol 2011;68:979–984.
4. Crawford TO, Paushkin SV, Kobayashi DT, Forrest SJ, Joyce CL, Finkel RS, et al; Pilot Study of Biomarkers for Spinal Muscular Atrophy Trial Group. Evaluation of SMN protein, transcript, and copy number in the biomarkers for spinal muscular atrophy (BforSMA) clinical study. PLoS One. 2012;7:e33572.
5. Prior TW, Krainer AR, Hua Y, Swoboda KJ, Snyder PC, Bridgeman SJ, et al. A positive modifier of spinal muscular atrophy in the SMN2 gene. Am J Hum Genet. 2009 Sep;85(3):408-13.
6. Wirth B, Karakaya M, Kye MJ, Mendoza-Ferreira N. Twenty-Five Years of Spinal Muscular Atrophy Research: From Phenotype to Genotype to Therapy, and What Comes Next. Annu Rev Genomics Hum Genet 2020;21:231–261.
7. Baioni MT, Ambiel CR. Spinal muscular atrophy: diagnosis, treatment and future prospects. J Pediatr (Rio J). 2010;86:261-70. English, Portuguese.
8. Verhaart, I.E.C, Robertson A, Wilson IJ, Aartsma-Rus A, Cameron S, Jones CC, et al. Prevalence, incidence and carrier frequency of 5q-linked spinal muscular atrophy - a literature review. Orphanet J Rare Dis. 2017 4;12:124.
9. Ogino S, Leonard DGB, Rennert H, Ewens WJ, Wilson RB. Genetic risk assessment in carrier testing for spinal muscular atrophy. Am J Med Genet 2002;110:301–7.
10. Konig K, Pechmann A, Thiele S, Walter MC, Schorling¨ D, Tassoni A, et al. De-duplicating patient records from three independent data sources reveals the incidence of rare neuromuscular disorders in Germany. Orphanet J Rare Dis 2019;14:152.
11. Zerres K, Rudnik-Schöneborn S, Forrest E, Lusakowska A, Borkowska J, Hausmanowa-Petrusewicz I. A collaborative study on the natural history of childhood and juvenile onset proximal spinal muscular atrophy (type II and III SMA): 569 patients. J Neurol Sci. 1997;146:67-72.
12. Zolgensma: SMA Progression https:// www.zolgensma.com/sma-progression. Accessed 8/9/2023.
13. Ninds.nid: Spinal Muscular Atrophy https:// www.ninds.nih.gov/health-information/disorders/ spinalmuscular-atrophy. Accessed 25/7/2023.
14. Prior TW, Leach ME, Finanger E. Spinal Muscular Atrophy. 2000 Feb 24 [updated 2020 Dec 3]. In: Adam MP, Mirzaa GM, Pagon RA, Wallace SE, Bean LJH, Gripp KW, Amemiya A, editors. GeneReviews® [Internet]. Seattle (WA): University of Washington, Seattle; 1993–2023.
15. Webmd: Spinal Muscular Atrophy Written by Mary Jo DiLonardo Medically Reviewed by Christopher Melinosky, MD on April 08, 2023 https://www.webmd.com/brain/spinal-muscular-atrophy.
16. Deguise M.O., De Repentigny Y., McFall E., Auclair N., Sad S., Kothary R. Immune dysregulation may contribute to disease pathogenesis in spinal muscular atrophy mice. Hum. Mol. Genet. 2017;26:801–819.
17. Aslesh T, Yokota T. Restoring SMN Expression: An Overview of the Therapeutic Developments for the Treatment of Spinal Muscular Atrophy. Cells. 2022 26;11:417.
18. Dhillon S. Risdiplam: First Approval. Drugs. 2020;80:1853–1858.
19. Burghes, A.H.M.; Beattie, C.E. Spinal muscular atrophy: Why do low levels of survival motor neuron protein make motor neurons sick? Nat. Rev. Neurosci. 2009, 10, 597–609.
20. Naryshkin, NA, Weetall M, Dakka A, Narasimhan J, Zhao X, Feng Z, et al. Motor neuron disease. SMN2 splicing modifiers improve motor function and longevity in mice with spinal muscular atrophy. Science. 2014 : 8;345 :688-693.
21. Ratni, H., Ebeling, M., Baird, J., Bendels, S., Bylund, J., Chen, K. S., et al. Discovery of Risdiplam, a selective Survival of Motor Neuron-2 (SMN2) gene splicing modifer for the treatment of spinal muscular atrophy (SMA). Journal of Medicinal Chemistry, 2018: 61: 6501–6517.
22. Ratni, H., Karp, G. M., Weetall, M., Naryshkin, N. A., Paushkin, S. V., Chen, K. S., et al. Specifc correction of alternative survival motor Neuron 2 splicing by small molecules: Discovery of a potential novel medicine to treat spinal muscular atrophy [Research Support, Non-US Gov't]. Journal of Medicinal Chemistry, 2016: 59, 6086-6100.
23. Bowerman, M., Becker, C. G., Yanez-Munoz, R. J., Ning, K., Wood, M. J. A., Gillingwater, T. H., et al. Therapeutic strategies for spinal muscular atrophy: SMN and beyond [Review Research Support, Non-U.S. Gov't]. Disease Models & Mechanisms, 2017:10, 943–954.
24. Sergott, R. C., Amorelli, G. M., Baranello, G., Barreau, E., Beres, S., Kane, S., et al. Risdiplam treatment has not led to retinal toxicity in patients with spinal muscular atrophy [Research Support, Non-U.S. Gov't]. Annals of Clinical and Translational Neurology, 2021 : 8, 54–65.
25. Bordet T, Berna P, Abitbol JL, Pruss RM. Olesoxime (TRO19622): A Novel Mitochondrial-Targeted Neuroprotective Compound. Pharmaceuticals (Basel). 2010 28;3:345-368.
26. Fahad A. Bashiri, Mohamad-Hani Temsah, Khalid Hundallah, Fahad Alsohime, Yazed AlRuthia. 2020 Update to Spinal Muscular Atrophy Management in Saudi Arabia. Sec. Pediatric Neurology Volume 9 - 2021
27. Wang CH, Bonnemann CG, Rutkowski A, Sejersen T, Bellini J, Battista V, et al. Consensus statement on standard of care for congenital muscular dystrophies. J Child Neurol. 2010: 25:1559–81.
28. Jianli Sun, Melissa A Harrington, Ben Porter. Sex Difference in Spinal Muscular Atrophy Patients - are Males More Vulnerable? J Neuromuscul Dis . 2023;10:847-867.
29. Verhaart IEC, Robertson A, Leary R, McMacken G, K¨onig K, et al. A multisource approach to determine SMA incidence and research ready population. Journal of Neurology.2017;264:1465-73.
30. Loke H, Harley V, Lee J. Biological factors underlying sex differences in neurological disorders. Int J Biochem Cell Biol. 2015;65:139-50.
31. Lopez-Lee C, Kodama L, Gan L. Sex Differences in Neurodegeneration: The Role of the Immune System in Humans. Biol Psychiatry. 2022;91:72-80.
32. Young LJ, Pfaff DW. Sex differences in neurological and psychiatric disorders. Front Neuroendocrinol. 2014;35:253-4.