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A Revolutionary Approach of Clinical Trials and Emerging Therapies for Myotonic Dystrophy

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Description

A complex genetic illness called Myotonic Dystrophy (DM) is characterized by myotonia, or the inability of muscles to relax after contraction, and progressive muscle weakening. It is brought on by the growth of repeating nucleotide sequences in particular genes, which has a variety of systemic implications. DM1 (Myotonic Dystrophy Type 1) and DM2 (Myotonic Dystrophy Type 2) are the two main forms of myotonic dystrophy. Developing successful treatments requires an understanding of the pathophysiology of these disorders. The Myotonic Dystrophy Protein Kinase (*DMPK*) gene, which is found on chromosome 19, is the source of Myotonic Dystrophy Type 1 (DM1), which is caused by an expansion of the Trinucleotide Repeat Expansion (CTG). While 5-35 CTG cycles are present in the normal gene, hundreds or thousands of sessions are present in DM1 [1]. A build-up of harmful RNA molecules occurs in the nucleus as a result of the enlarged CTG repeats. Regular Ribonucleic Acid (RNA) splicing is interfered with by these RNA foci, which sequester vital splicing factors. In addition to causing aberrant protein synthesis, this also exacerbates symptoms such as muscle weakness. On chromosome 3, the Cellular Nucleic Acid Binding Protein (*CNBP*) gene (CCHC-type zinc finger nucleic acid binding protein) has an extension of the Caprylic Capric Triglyceride (CCTG) tetranucleotide repetition. This expansion is linked to Myotonic Dystrophy Type 2 (DM2) [2-3].

Like DM1, the enlarged repetitions generate toxic RNA that stows away splicing components, causing splicing to go out of control and malfunctioning proteins to be produced. Compared to DM1, DM2 typically manifests with milder symptoms, however it can still be extremely disabling. Muscle fiber abnormalities, such as myopathic alterations and the presence of central nuclei in muscle fibers, are characteristics shared by both forms of myotonic dystrophy. Muscle atrophy and weakening are caused by the loss of muscle fibers and their replacement by fibrous and fatty tissue [4]. Prolonged muscular contractions and myotonia, which are characteristic symptoms of the condition, are revealed by electromyographic investigations. Myotonic dystrophy can cause symptoms in the muscles as well as other organ systems. Heart conduction disorders, glaucoma insulin resistance, and gastrointestinal issues can all occur with DM1. In addition, heart involvement and, less commonly, cataracts are observed in DM2. The extensive expression of the mutant RNA and protein products in a variety of tissues contributes to the systemic consequences [5].

The purpose of Antisense Oligonucleotides (ASOs) is to selectively attach to the harmful RNA that the enlarged repeats create and encourage its breakdown. Preclinical investigations on DM1 have demonstrated the potential of ASOs targeting the enlarged CTG repeat RNA, since they reduce RNA foci and improve splicing anomalies. ASOs that target DM2's enlarged CCTG repeats are also being researched. Small RNA molecules are used in RNA interference (RNAi) to target and destroy particular mRNA transcripts. Treatments based on RNA interference (RNAi) are being developed to lower the harmful RNA levels in myotonic dystrophy. The goal of this strategy is to reduce splicing factor sequestration and restore regular RNA processing [6]. The CRISPR/Cas9 technology makes precise genomic sequence editing possible. In order to directly fix the enlarged CTG or CCTG repeats in the DMPK and CNBP genes, researchers are investigating the use of Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR) [7]. This strategy, while still in its infancy, has the potential to target the underlying source of the illness and offer a long-term remedy. To repair the erroneous splicing brought on by the deadly RNA, researchers are looking into small compounds that modulate splicing. These substances seek to enhance the synthesis of useful proteins by reestablishing the proper splicing of precursor mRNA (pre-mRNAs) [8].

Clinical trials are being conducted on medications for DM1, including losmapimod, to determine how well they work to improve muscular function and lessen myotonia. Small compounds known as pharmacological chaperones assist in stabilizing and enhancing the performance of misfolded proteins. These substances may be able to restore normal cellular activity and compensate for the functional deficiencies brought on by mutant proteins in myotonic dystrophy. The goals of gene therapy techniques are to either mute the expression of the mutant gene or replace the damaged gene with a functional copy. This would entail delivering therapeutic genes or RNA molecules to muscle cells through viral vectors for DM1 and DM2 [9]. According to preclinical research, gene therapy can address a few of the genetic abnormalities linked to myotonic dystrophy. For people with myotonic dystrophy to manage their muscular weakening and preserve their mobility, physical treatment is essential. Programmings for exercise are individualized for each patient can help increase the function and strength of their muscles [10]. For individuals suffering from myotonic dystrophy, it is crucial to monitor and treat cardiac symptoms, including as conduction abnormalities and arrhythmias. To address cardiac problems, further interventions such as heart rate monitors may be necessary [11]. Multidisciplinary treatment is necessary for systemic symptoms like insulin resistance and glaucoma. Individuals with these symptoms may have an overall higher quality of life after receiving treatment.

Conclusion

Myotonic dystrophy is a complicated hereditary illness that affects several organ systems and muscle function. Expanded nucleotide repeats produce toxic RNA that disrupts splicing and results in the generation of defective proteins, which is the pathophysiology involved. RNA-based medicines, gene editing technologies, and small compounds are being used as emerging treatments for addressing the underlying molecular abnormalities. Furthermore, supportive therapies are essential for symptom management and quality of life enhancement. Myotonic dystrophy may not progress as expected if more precise and potent treatments are developed, which could improve patient outcomes.

References

1. Liao Q, Zhang Y, He J, Huang K (2022) Global prevalence of myotonic dystrophy: an updated systematic review and meta-analysis. Neuroepidemiology 56:163-173.
2. Liquori CL, Ricker K, Moseley ML, Jacobsen JF, Kress W, et al. (2001) Myotonic dystrophy type 2 caused by a CCTG expansion in intron 1 of ZNF9. Science 293:864-867.
3. Ho G, Carey KA, Cardamone M, Farrar MA (2019) Myotonic dystrophy type 1: Clinical manifestations in children and adolescents. Arch Dis Child 104:48-52.
4. Zanigni S, Evangelisti S, Giannoccaro MP, Oppi F, Poda R, et al. (2016) Relationship of white and gray matter abnormalities to clinical and genetic features in myotonic dystrophy type 1. Neuroimage Clin 11:678-685.
5. Weber YG, Roebling R, Kassubek J, Hoffmann S, Rosenbohm A, et al. (2010) Comparative analysis of brain structure, metabolism, and cognition in myotonic dystrophy 1 and 2. Neurology 74:1108-1117.
6. Yoo WK, Park YG, Choi YC, Kim SM (2017) Cortical thickness and white matter integrity are associated with CTG expansion size in myotonic dystrophy type I. Yonsei Med J 58:807-815.
7. Schilling KG, Blaber J, Huo Y, Newton A, Hansen C, et al. (2019) Synthesized b0 for diffusion distortion correction (Synb0-DisCo). Magn Reson Imaging 64:62-70.
8. Smith SM, Jenkinson M, Johansen-Berg H, Rueckert D, Nichols TE, et al. (2006) Tract-based spatial statistics: voxelwise analysis of multi-subject diffusion data. Neuroimage 31:1487-1505.
9. Okkersen K, Monckton DG, Le N, Tuladhar AM, Raaphorst J, (2017) Brain imaging in myotonic dystrophy type 1: A systematic review. Neurology 89:960–969.
10. Franc DT, Muetzel RL, Robinson PR, Rodriguez CP, Dalton JC, et al. (2012) Cerebral and muscle MRI abnormalities in myotonic dystrophy. Neuromuscul Disord 22:483–491.
11. Winblad S, Lindberg C, Hansen S (2006) Cognitive deficits and CTG repeat expansion size in classical myotonic dystrophy type 1 (DMI). Behav Brain Funct 2:16.