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AYURVEDIC MANAGEMENT OF GNE MYOPATHY: A COMPREHENSIVE APPROACH

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ABSTRACT

Hereditary inclusion body myopathy (HIBM), or GNE Myopathy, is an uncommon hereditary neuromuscular disorder that predominantly impacts the skeletal muscles. The aim of this article is to provide a comprehensive understanding of the pathophysiology of GNE Myopathy, including its effects on skeletal muscle function and potential treatment approaches, with an emphasis on Ayurvedic methods. Progressive muscle weakness and atrophy characterise GNE Myopathy, which results in substantial disability and a diminished quality of life. Gaining insight into the molecular mechanisms that underlie this disorder is of utmost importance in order to formulate efficacious therapeutic interventions, notwithstanding its infrequency. Ayurveda, the conventional Indian medical system, provides comprehensive strategies for the treatment of neuromuscular disorders and other ailments. The purpose of this research is to investigate the potential of Ayurvedic treatments to alleviate the symptoms of GNE myopathy and enhance the overall health of patients.

KEYWORDS: Hereditary Inclusion Body Myopathy (HIBM), GNE Myopathy, Skeletal Muscle Dysfunction, Ayurvedic Treatment.

INTRODUCTION

Hereditary Inclusion Body Myopathy (HIBM), more commonly referred to as GNE Myopathy, is an uncommon neuromuscular disorder distinguished by the progressive atrophy and weakness of muscles.[1][2] It is caused by mutations in the GNE gene, which encodes for an enzyme that is essential for the synthesis of sialic acid. Sialic acid is indispensable for glycosylation, the process by which sugar molecules are attached to proteins.[3] Glycosylation is critical for the operation of muscle cells, as it facilitates adhesion, communication, and signalling pathways that are necessary for energy production and muscle contraction. Enzyme deficiency caused by genetic mutations ultimately results in dysfunctional muscle cells and a progressive decline in muscle strength and mass.

The manifestation of the condition is contingent upon the inheritance of two defective copies of the GNE gene, which follows an autosomal recessive inheritance pattern.[4] Although frequently asymptomatic, carriers of a single mutated copy are capable of transmitting the mutation. Typically manifesting in early adulthood, the severity and timing of symptoms vary among those affected. Muscle weakness and atrophy, specifically in the lower extremities (legs, hips, and shoulders), as well as muscle mass loss, are prevalent complications that impede performance of strength-based activities. Certain individuals may encounter foot drop, which obstructs the lifting of the front foot and gives rise to a discernible gait.

As there is currently no known cure for GNE Myopathy, symptom management and quality of life improvement are the primary concerns. Medication for the relief of symptoms, physical therapy to preserve muscle strength and flexibility, and assistive devices such as orthotics or braces to support weakened muscles comprise the treatment regimen.[5] Ayurveda, an ancient medical system with its roots in India, presents a comprehensive remedy system that prioritises individualised treatments that are customised to suit the unique constitutions of each patient. Gaining knowledge about the pathophysiology of GNE Myopathy and investigating Ayurvedic treatment modalities may yield novel perspectives on the efficient management of this condition.

Symptoms[6]

GNE Myopathy affects skeletal muscles, which are essential for movement and stability. As muscle strength and function decline, symptoms appear in the second and third decades of life. This gradual progression can cause significant physical disability and lower quality of life. Below, we describe GNE Myopathy symptoms:

I. **Progressive Muscle Wasting:** GNE Myopathy causes muscle mass and strength to decrease. Before moving to proximal muscles, the condition usually starts in distal muscles like those around the ankles and feet. Muscle wasting causes weakness and function loss.

II. **Severe Disability:** As the disease progresses, daily tasks may become difficult. Muscle loss can cause severe disability, requiring home modifications, assistive devices, and possibly full-time care.

III. **Bilateral Foot Drop:** Weakness in the muscles that lift the front of the foot causes bilateral foot drop, an early sign of GNE Myopathy. This condition makes walking difficult and may cause a high-stepping gait or tripping and falling.

IV. GNE-related muscle weakness disrupts gait. Myopathy often changes walking patterns. Waddling or high-stepping can impair mobility and increase fall risk.

V. **Decreased Stability:** Weakened leg and foot muscles can make it hard to stand or walk without help. Lack of stability often causes a fear of standing or walking, limiting mobility and independence.

VI. **Frequent Falls:** Foot drop, disturbed gait, and decreased stability increase fall risk. Falls can cause injuries, complicating GNE Myopathy treatment.

VII. Due to thigh and hip muscle weakness, climbing stairs may become harder as the condition progresses. This symptom can severely limit independence and access to many environments.

VIII. **Running:** Progressive muscle weakness makes running and walking difficult. Running and other leg-strengthening activities may decline early in the disease.

IX. Muscle weakness, especially in the thighs and buttocks, can make it hard to stand up from a seated position. This problem may require assistive devices or help from others.

Ayurvedic approach[7]

Ayurveda, an ancient Indian holistic medical system, elucidates the nature of diseases by considering the equilibrium or disequilibrium of the doshas (Vata, Pitta, and Kapha), the body's fundamental principles; additionally, the condition of the dhatus (body tissues) and malas (waste products) is taken into consideration. The principle of "Mamsa dhatu gata Vata," which pertains to a state in which the Vata dosha (one of the three primary doshas responsible for bodily communication and movement) becomes vitiated, resulting in the deterioration or depletion of muscle tissues (Mamsa dhatu kshaya), provides a distinctive perspective from Ayurveda regarding myopathies, including conditions like GNE Myopathy.

- **Comprehension of Vata Dosha and Mamsa Dhatu:** The human body is composed of seven dhatus, as described in Ayurveda: Rasa (blood), Rakta (plasma), Mamsa (muscle tissue), Medha (adipose or fat tissue), Asthi (bones), Majja (bone marrow), and Shukra (sperm or reproductive tissue). These dhatus are essential for the preservation of optimal physiological processes. Muscle tissue, or mamsa dhatu, is especially vital for movement and physical strength. Vitiation or depletion of Mamsa dhatu (Mamsa dhatu dushti or kshaya) can result in the development of conditions such as Mamsa shosha (muscle wasting), which presents itself as weakness and limited mobility, similar to the symptoms observed in GNE Myopathy.

Vata dosha, which is comprised of the elements dry, light, cold, and mobile, is intrinsically associated with bodily functions such as communication, movement, and the functioning of the nervous system. A disruption in the body's equilibrium can result from vitiated Vata, which can affect tissues such as Mamsa dhatu and induce conditions of wasting or depletion.

- **Therapeutic Aspects of Myopathies:** Regarding GNE Myopathy and analogous conditions, Ayurveda identifies "Mamsa dhatu gata Vata" as the fundamental cause—virtually speaking, a deterioration of Vata that results in the depletion of muscle tissue. Due to its genetic underpinnings, GNE Myopathy is classified as a "Adhi-Bala pravritta vyadi" (a hereditary ailment) and placed in the "Asadhya roga" category (diseases that are exceedingly challenging or uncurable) by Ayurveda. Ayurveda, on the other hand, provides methods for managing the condition with the objective of extending muscle function and enhancing quality of life.

Management of GNE Myopathy

1. **Conventional management[8]:** In spite of the absence of a definitive cure for GNE Myopathy, treatment approaches are designed to alleviate symptoms and impede the disease's progression. These strategies consist of:

Physiotherapy and Optimal Muscle Movement: Patients diagnosed with GNE Myopathy must adhere to consistent and meticulously customised physiotherapy regimens. The primary objective is to preserve optimal muscle function, avert contractures (which are irreversible afflictions of the muscles or joints), and effectively address muscle weakness while preventing additional harm. Striking a balance between adequately engaging muscles to preserve strength and preventing overuse, which can hasten muscle atrophy and wasting, is a

nuanced task. Sufficient physical activity has the potential to promote muscle strength maintenance and impede the advancement of muscle weakness.

Enzyme replacement therapy (ERT): ERT seeks to supplement the malfunctioning or deficient enzyme caused by GNE gene mutations, has been investigated as a potential treatment for GNE myopathy. The enzyme should, in theory, aid in the restoration of healthy muscle function or the slowing of the disease's progression. ERT research for GNE myopathy, however, has produced mixed results. Although a few studies have reported a slight enhancement in muscular strength, the overall impact of these results has been inconsequential and lacks sufficient magnitude to justify further financial investment in this methodology as an independent therapeutic approach. The primary obstacle is not solely the efficient transportation of the enzyme to the muscle cells, but also the verification of its proper functionality within said cells. In addition, due to the intricate nature of the disease mechanism, enzyme replacement may not be sufficient to rectify all pathological aspects of GNE Myopathy.

Due to its limited efficacy, enzyme replacement therapy research was discontinued, highlighting the need for a multifaceted approach to the treatment of GNE Myopathy. Alternative treatments could consist of gene therapy to rectify the fundamental genetic abnormality, innovative pharmaceuticals designed to improve muscle growth or function, or strategies to augment sialic acid concentrations in muscle cells. Furthermore, nutritional support, adaptive devices, and occupational therapy are all essential components of supportive care that significantly contribute to disease management and the enhancement of the affected population's quality of life.

2. **Ayurvedic Management[9]:** In the context of GNE Myopathy and other conditions of a similar nature, Ayurveda considers "Mamsa dhatu gata Vata" to be the underlying cause. This condition is essentially a vitiation of Vata that will result in the depletion of muscle tissue. Considering the genetic basis of GNE Myopathy, Ayurveda classifies it as a "Adhi-Bala pravritta vyadi" (a disease that is inherited from one's parents), which places it under the category of "Asadhya roga" (diseases that are extremely difficult or impossible to cure). Nevertheless, Ayurveda provides methods for the management of the condition, with the objective of extending the function of the muscles and enhancing the quality of life.

The treatment plan in Ayurveda for conditions such as GNE Myopathy focuses on both calming the vitiated Vata and nourishing the Mamsa dhatu in order to prevent further depletion of the dhatu. Because Vata vitiation and tissue depletion feed into each other, creating a cycle that needs to be addressed holistically, this dual approach is essential because it treats both of these conditions simultaneously.

Various Methods of Treatment

1. Snehana, also known as oleation therapy, is a technique that has the potential to help balance the Vata dosha, nourish tissues, and facilitate the removal of toxins from the body. It can be performed both internally and externally using medicated ghee and oils.
2. Following the completion of Snehana, Swedana, also known as steam therapy or sudation, is a technique that helps further pacify Vata and remove toxins through the process of inducing sweating. The reduction of stiffness and the improvement of mobility are two areas in which this is especially helpful.
3. Specific herbal preparations that are known for their rejuvenative properties can assist in nourishing and strengthening muscle tissues. Rasayana, also known as rejuvenation therapy, is a form of treatment. Withania somnifera, also known as Ashwagandha, and Sida cordifolia, also known as Bala, are two herbs that are frequently recommended due to their powerful anti-Vata and muscle-strengthening properties.
4. Panchakarma, also known as detoxification therapy, includes procedures such as Vasti, which are medicated enemas. These procedures are particularly effective in treating Vata disorders and can be helpful in the management of conditions such as GNE Myopathy. They do this by directly nourishing and rejuvenating the colon, which is the primary site of Vata.
5. Diet and Lifestyle: It is recommended to consume a diet that is in harmony with Vata and that nourishes the dhatus. Additionally, it is recommended to make adjustments to one's lifestyle that strive to reduce stress and promote stability and warmth within the body.

Herbal medicine[10]

- **Ashwagandha Ghrit:** Ashwagandha ghrit is an ancient ayurvedic remedy prepared with ghee and primarily composed of Withania somnifera. Ashwagandha, alternatively referred to as "Indian ginseng," is a botanical specimen that is rich in sitoindosides, withanolides, and adaptogens. Moreover, it aids in the development of muscular and bodily strength. Utilising ghee as a medium effectively promotes the drug's digestion and absorption, thereby accelerating the restoration of muscle functions.

- **Musli:** Pharmacological applications include Gokshura (Tribulus terrestris) and Musli (Chlorophytum borivilianum). The standard extracts of both substances are encapsulated in capsules composed entirely of vegetarian ingredients. Musli, which is known to increase muscle strength, nourish the muscles, and promote overall health, is composed of more than twenty-five alkaloids. Steroidal saponin-containing Gokshura is an exceptional immunomodulator and fortifying agent.
- **Boswellia plus curcumin:** Two remarkable medications, Shallaki (Boswellia serrata) and Haridra (curcuma longa, or turmeric), possess an extensive array of health advantages. There are numerous benefits associated with turmeric, and shallaki functions as a tonic that replenishes the body, promoting overall health and preventing degenerative changes. A concurrent use of pharmaceuticals containing phytoconstituents (e.g., curcumin, Acetyl-11-keto-β-boswellic acid) has the potential to impede the progression of the disease and enhance overall well-being.
- **Yograj Guggul:** Yograja guggul is an Indian traditional medicine that has been practiced for generations.A polyherbal tablet containing chitraka (Plumbago zeylanica), pippali (Piper longum), Yamani (Trachyspermum ammi), and other botanicals is being described. The 29 phytoconstituents added to this medication assist in vata dosha balance, muscular strength enhancement, and general health improvement.
- **Atirasadi Churna:** This extraordinary formulation contains, among other things, Ashwagandha (Withania somnifera), Nutmeg (Myristica fragrans), Kali Musli (Curculigo orchioides), Safed Musli (Chlorophytum borivilianum), Gokshura (Tribulus terrestris), and others. This powdered polyherbal medicine contains a multitude of active constituents, including alkaloids, saponins, and withanolides, among others, which can assist in muscle regeneration, immunity enhancement, and body rejuvenation.
- **Rasraj Ras:** Tablet form of a traditional herbal mineral remedy adapted from the Siddha yoga sangraha. This medication's efficacy in treating neuromuscular disorders has been demonstrated over centuries of use. It exhibits significant immunomodulatory, analgesic, and antioxidant properties.
- **Balaswagandhadi Thailam:** Utilised topically, this medicinal oil is formulated with Bala (Sida cordifolia), Ashwagandha (Withania somnifera), and numerous other substances. Asheswagandha and balsa contain natural steroids that hasten the healing process. In addition to nourishing and fortifying the bones, muscles, and joints, the oil appeases the Vata dosha.

6. CONCLUSION

GNE Myopathy poses considerable difficulties in the field of clinical management, requiring the implementation of a multidisciplinary strategy to tackle its intricate pathophysiology and incapacitating symptoms. In contrast to conventional treatments which primarily target symptomatic relief and supportive care, Ayurveda presents comprehensive interventions that seek to restore equilibrium and foster optimal health. Patients who incorporate Ayurvedic principles and therapies into their GNE Myopathy management may observe enhancements in their physical strength, mobility, and overall well-being. Additional investigation and clinical trials are necessary to substantiate the effectiveness and safety of Ayurvedic treatments for neuromuscular disorders.

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