



Original Article

Therapeutic Challenges and Opportunities in Myopathy Management: A Narrative Review

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ABSTRACT

Background: Myopathies are a heterogeneous group of muscle disorders that affect more than 1.7 billion people worldwide and present significant therapeutic challenges because of their diverse etiologies, clinical manifestations, and varying degrees of disease severity.

Methods: This narrative review examines current therapeutic approaches for myopathies, including herbal remedies, complementary therapies such as acupuncture and massage, physiotherapy, nutritional interventions, and emerging gene therapies. Herbal remedies and complementary therapies may provide symptomatic relief for some patients, whereas physiotherapy helps preserve muscle function and improve physical performance. Nutritional interventions support overall health and may contribute to disease management, while gene therapies offer promising strategies to target the underlying genetic defects in inherited myopathies. However, the effectiveness of these interventions varies, and robust clinical evidence supporting many of these approaches remains limited.

Results: Herbal remedies and complementary therapies may provide symptomatic relief for some patients, whereas physiotherapy helps preserve muscle function and improve physical performance. Nutritional interventions support overall health and may contribute to disease management, while gene therapies offer promising strategies to target the underlying genetic defects in inherited myopathies. However, the effectiveness of these interventions varies, and robust clinical evidence supporting many of these approaches remains limited.

Conclusion: This review highlights the need for future research to prioritize large-scale, high-quality clinical trials to establish the safety and efficacy of existing and emerging therapies, develop personalized treatment strategies tailored to individual patient characteristics, and improve access to innovative therapeutic options. Addressing these challenges may enhance the clinical management of myopathies and ultimately improve patient outcomes and quality of life across diverse populations.

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Introduction

Myopathy encompasses a heterogeneous group of muscle disorders characterized by progressive muscle weakness and degeneration. These conditions substantially impair patients' quality of life by limiting mobility, restricting the performance of daily activities, and reducing overall physical functioning and well-being [1]. The societal burden of myopathies is considerable and includes not only the direct healthcare costs associated with diagnosis, treatment, and long-term management but also indirect costs resulting from reduced productivity, diminished workforce participation, and the need for ongoing support and caregiving for affected individuals and their families [2].

Despite advances in understanding myopathy pathophysiology, effective treatment options remain limited for many forms of the disease, underscoring the urgent need to develop novel therapeutic strategies. This narrative review examines the potential of conventional therapies, emerging therapeutic approaches, and complementary interventions to manage myopathy and improve patient outcomes. It also summarizes the current evidence on the efficacy and safety of these treatment modalities, identifies important gaps in the literature, and outlines priorities for future research. A comprehensive understanding of the benefits and limitations of available therapies is essential for developing effective, evidence-based, and accessible treatment strategies for individuals living with these debilitating disorders.

Myopathy

Myopathy is a broad term that refers to a group of disorders affecting skeletal muscle. Skeletal muscles account for approximately 40% of total body mass and play a vital role in performing daily activities and voluntary movements [3]. More than 1.7 billion people worldwide are affected by musculoskeletal disorders, making them the second leading cause of disability globally [4, 5]. Myopathies may be either inherited or acquired. Inherited myopathies include congenital, mitochondrial, and metabolic myopathies, as well as muscular dystrophies. Acquired myopathies develop later in life and include inflammatory myopathies, toxic myopathies, and endocrine myopathies [6]. Because myopathies have diverse etiologies and clinical manifestations, their treatment and symptom management require individualized therapeutic approaches tailored to each patient's condition.

Pharmacotherapy

Pharmacological management varies considerably depending on the type of myopathy, as these disorders have diverse etiologies and clinical manifestations. For inflammatory myopathies, such as dermatomyositis, first-line treatment typically consists of corticosteroids in combination with immunosuppressive agents, including methotrexate or azathioprine, to achieve a steroid-sparing effect [7]. In selected cases, intravenous immunoglobulin (IVIg) and biologic agents, such as rituximab, are used as second-line therapeutic options [8].

For certain metabolic myopathies, enzyme replacement therapies, such as alglucosidase alfa, have been approved and have demonstrated clinical benefit in specific patient populations [9]. In addition, a study by Bak, Moon, et al. (2023) reported that the concomitant use of metformin and statins was associated with a reduced risk of myopathy, with no significant influence of specific statin agents or patient characteristics on this association [10]. These findings suggest that metformin may mitigate statin-induced muscle toxicity.

Advances in precision medicine, including genetic screening, drug combination analyses, and the development of therapies targeting mitochondrial dysfunction and oxidative stress, have created new opportunities for improving the management of myopathies. For example, interventions such as L-carnitine supplementation may help reduce treatment-related adverse effects and improve clinical outcomes in selected patients [11].

Gene therapy

The development of gene therapy offers a promising strategy for restoring deficient or dysfunctional proteins in inherited muscle disorders, such as X-linked myotubular myopathy (XLMTM). By targeting the underlying genetic defects, gene therapy has the potential to transform current treatment paradigms and significantly improve patient outcomes [12].

Advances in molecular diagnostics have further supported the implementation of precision medicine in myopathies. For example, whole-exome sequencing has proven effective in diagnosing congenital myopathies, as demonstrated in a case in which a neonate was diagnosed with central core myopathy after initially presenting with symptoms that were suspected to be neurological sequelae of birth asphyxia [13]. Similarly, a maternally inherited mutation in the mt-tRNA^{Glu} gene has been identified in patients with benign cytochrome *c* oxidase deficiency myopathy, a condition characterized by the potential for spontaneous recovery during infancy [14].

Preclinical and early clinical studies have demonstrated that gene therapy can restore myotubularin expression in skeletal muscle, a critical therapeutic target in XLMTM. Furthermore, advances in understanding and management of respiratory complications associated with inherited myopathies have spurred the development of novel therapeutic approaches. These include gene therapy, enzyme replacement therapy, and pharmacological agents that modulate downstream molecular pathways, all of which offer promising opportunities for improving disease management and long-term outcomes [15].

Despite these advances, several important challenges remain. These include difficulties in distinguishing patients with favorable prognoses from those with progressive or life-threatening disease, limitations in predicting long-term therapeutic responses, and the absence of effective targeted treatments for several forms of myopathy [16].

Physiotherapy

In the absence of disease-modifying therapies or other effective treatment options, physiotherapy plays a crucial role in the symptomatic management of myopathies,

Electrical Stimulation

Electrical stimulation, particularly transcutaneous electrical neuromuscular stimulation (TENMS) and neuromuscular electrical stimulation (NMES), has been investigated as a potential therapeutic approach for reducing the incidence and severity of myopathy, particularly in critically ill patients. Evidence suggests that NMES can improve muscle strength and function, enhance muscle blood flow, and promote angiogenesis, thereby helping to preserve muscle mass and physical function in patients admitted to intensive care units (ICUs) [17].

In addition, novel rehabilitation technologies have been developed to enhance motor recovery. One such approach combines mechanical assistance with electrical stimulation to facilitate upper-limb rehabilitation in individuals with neurological disorders. This device incorporates a robotic support system equipped with motion sensors and electrical stimulation electrodes that continuously adjust the level of mechanical assistance and electrical stimulation in real time according to the user's movements, thereby promoting more effective motor recovery [18].

In the context of critical illness myopathy (CIM), chronic supramaximal electrical stimulation (ES) has been investigated as a potential therapeutic intervention. This approach has been evaluated in a rat model, demonstrating that ES may attenuate muscle mass loss and improve muscle function, although the

underlying mechanisms have not yet been fully elucidated [19].

Overall, electrical stimulation has shown considerable promise in the management of myopathy, particularly among critically ill patients, by helping to reduce muscle atrophy and preserve muscle function [17]. However, several challenges remain, including the determination of optimal stimulation parameters, variability in patient responses, and the potential risk of complications such as rhabdomyolysis [20].

Exercise

Exercise is a fundamental component of the rehabilitation and long-term management of myopathies. Strength training and range-of-motion exercises can help prevent muscle atrophy, preserve joint mobility, and improve functional capacity [21]. In addition, high-resistance strength training performed at submaximal and near-maximal intensities has demonstrated short-term benefits in individuals with slowly progressive myopathic disorders, although its long-term effects remain to be established [21, 22].

Exercises targeting balance and coordination can improve mobility and reduce the risk of falls [23]. Regular exercise may also help prevent respiratory complications, which are common in patients with myopathies, and reduce fatigue, thereby improving overall physical function [24].

In inflammatory myopathies, such as dermatomyositis and polymyositis, physiotherapy plays an essential role during both the active inflammatory and recovery phases of the disease [25]. During the active phase, rehabilitation focuses primarily on preventing joint contractures and providing respiratory physiotherapy, whereas during the recovery phase, the emphasis shifts toward strengthening the remaining functional muscle fibers and managing corticosteroid-induced myopathy [26].

Furthermore, musculoskeletal physiotherapy has demonstrated beneficial effects in improving physical symptoms among patients recovering from post-COVID-19 syndrome [26]. Nevertheless, additional research is needed to develop rehabilitation programs that enhance patient adherence and engagement, particularly by incorporating gradual interventions, such as initial stretching-based therapy, for individuals with severe muscle weakness [27].

Complementary Therapies

Complementary therapies play an important role in the symptomatic management of myopathies by helping to alleviate symptoms, reduce pain, and improve patients' overall quality of life. Because most inherited myopathies currently have no curative treatment, these approaches represent an important area

for future research. The following complementary therapies have demonstrated promising results in previous studies.

Acupuncture

Acupuncture has shown promising therapeutic potential in the management of certain forms of myopathy. In patients with sepsis-induced myopathy (SIM), acupuncture may improve muscle structure and function while enhancing performance in activities of daily living [28]. Similarly, in diabetic myopathy, electroacupuncture has been shown to influence the expression of proteins involved in muscle function in diabetic mouse models, suggesting a potential mechanism through which acupuncture may promote muscle health [29].

In addition, several traditional East Asian medicine interventions, including acupuncture, have demonstrated beneficial effects in alleviating symptoms associated with mitochondrial encephalomyopathy, lactic acidosis, and stroke-like episodes (MELAS) syndrome, indicating that acupuncture may serve as a complementary therapeutic approach for managing this condition [30].

Despite these encouraging findings, the biological mechanisms underlying the therapeutic effects of acupuncture remain incompletely understood. Recent studies have highlighted the potential involvement of microRNAs and Piezo ion channels in mediating the physiological effects of acupuncture, suggesting that these molecular pathways may play an important role in explaining its therapeutic benefits in myopathies and other disorders [31, 32].

Massage Therapy

Massage therapy has demonstrated potential as a complementary intervention in the management of certain myopathies. In one case report involving a patient with cervical ventroflexion, an integrative treatment approach that included Tui-na massage was well tolerated and was associated with improvements in muscle recovery and pain relief [33]. Massage therapy may also help alleviate muscle pain and stiffness, thereby contributing to improved comfort and functional well-being [34].

Another case report involving a bird with cervical myopathy described an integrative rehabilitation program combining acupuncture, Tui-na massage, and therapeutic exercises. This multimodal approach was well tolerated and was associated with improvements in clinical status, including reduced serum enzyme levels and enhanced mobility [33].

There is a valuable opportunity to investigate further and validate the role of massage therapy in promoting functional recovery and improving the quality of life of

individuals with myopathies. To strengthen the evidence base, well-designed, large-scale clinical trials are needed to evaluate the safety, efficacy, and long-term benefits of massage therapy across different types of myopathy. Establishing robust clinical evidence could facilitate its broader integration into multidisciplinary rehabilitation programs and increase its acceptance among healthcare professionals. Furthermore, advances in this field may encourage collaboration among clinicians, biomedical engineers, and industry partners to develop innovative rehabilitation technologies, such as specialized massage devices and virtual reality-based therapeutic systems [35, 36].

Nutrition and Diet

In the context of supportive care, nutritional interventions and vitamin supplementation play important roles in maintaining muscle health and optimizing clinical outcomes in patients with myopathies. For example, insulin-like growth factor-1 (IGF-1) plays a key role in attenuating muscle wasting associated with diabetes and other catabolic conditions. Enhancing IGF-1 signaling may help counteract muscle atrophy by promoting muscle regeneration and protein synthesis, thereby contributing to improved muscle mass and function [37].

In addition, specific nutritional interventions have shown promise in certain inherited myopathies. For instance, L-tyrosine supplementation has been reported to improve muscle strength in infants with nemaline myopathy, suggesting that targeted nutritional strategies may serve as valuable adjunctive therapies for this rare neuromuscular disorder [38].

Vitamin D plays an important role in muscle regeneration by regulating the expression of myogenic regulatory factors, including myogenic differentiation 1 (MYOD) and myogenin, which are essential for muscle cell proliferation and differentiation [39]. Similarly, selenium (Se) is an essential micronutrient that contributes to normal muscle function and has been recognized for its role in the prevention of several muscle disorders, including nutritional muscular dystrophy and Keshan disease, both of which are associated with selenium deficiency [40].

In addition, dietary patterns such as the Mediterranean and vegan diets are rich in anti-inflammatory compounds that may help reduce inflammation associated with muscle disorders. Emerging evidence also suggests that combinations of multiple micronutrients may improve symptoms in conditions such as heart failure, raising the possibility that similar nutritional strategies could benefit patients with myopathies. However, further well-designed

clinical studies are required to confirm their efficacy and safety in this population [41].

Herbal Treatments

Herbal medicine is widely used as a complementary approach for the management of myopathies in many countries, including China, Thailand, Turkey, and Pakistan. Its popularity is largely attributed to its relatively low cost, perceived lower incidence of adverse effects compared with some conventional medications, and its long-standing acceptance within local healthcare traditions and communities [42].

Among the most extensively studied herbal compounds is curcumin, a bioactive constituent of turmeric with well-documented anti-inflammatory and antioxidant properties. Curcumin may help reduce inflammation in inflammatory myopathies, thereby alleviating pain and improving functional outcomes [43]. Astragalus is another medicinal herb that has been reported to reduce oxidative stress and modulate immune responses, potentially promoting muscle cell regeneration and enhancing energy metabolism [44]. Likewise, ginseng, a traditional Chinese medicinal herb, has been shown to stimulate the production of growth factors and support muscle regeneration [45].

Despite these promising findings, ensuring the quality, safety, and consistency of herbal products remains essential for their effective clinical application. Quality control techniques, such as high-performance liquid chromatography (HPLC), are valuable for verifying the identity, purity, and chemical composition of herbal preparations. In addition, standardized cultivation, extraction, and manufacturing processes are critical for minimizing variability and reducing the risks of contamination, adulteration, or inconsistent active-compound concentrations.

Conclusion

This review provides an overview of a variety of therapeutic approaches for the management of myopathies, a diverse group of debilitating muscle diseases that affect millions of people worldwide. The available treatment options vary considerably depending on the specific type of myopathy, its underlying causes, and the severity of its symptoms. The use of gene therapy, pharmacological therapy, acupuncture, electrical stimulation, massage therapy, physiotherapy, and a healthy diet offers promising approaches for treating myopathy and maintaining functional ability and quality of life.

Future research should focus on: (1) understanding the mechanisms of action of promising therapies; (2)

conducting large-scale, well-designed clinical trials to validate the efficacy and safety of various treatments; (3) developing personalized treatment strategies for specific myopathy subtypes and patient characteristics; and (4) improving access to effective and cost-efficient treatments for individuals affected by these disorders. Only through collaboration across multiple disciplines can we hope to improve the lives of people living with myopathy significantly.

Conflicts of interest

The authors declare no conflicts of interest.

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