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Review Article

Lifestyle Modification Rehabilitation and Pharmacotherapy in Multiple Sclerosis

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ABSTRACT

Multiple sclerosis (MS) is a chronic, immune-mediated neurological disorder characterized by inflammation, demyelination, axonal damage, and progressive neurodegeneration, resulting in a wide range of physical, cognitive, emotional, and functional impairments. Comprehensive management of MS requires an individualized and multidisciplinary approach integrating lifestyle modification, rehabilitation, and pharmacotherapy. Lifestyle interventions, including regular physical activity and exercise, healthy dietary practices, adequate sleep, stress management, smoking cessation, and maintenance of healthy body weight, may contribute to improved physical function, fatigue, psychological well-being, and quality of life. Rehabilitation is an essential component of long-term MS care and includes physiotherapy, occupational therapy, cognitive rehabilitation, speech and language therapy, balance and mobility training, and strategies for managing fatigue, spasticity, pain, and other disabling symptoms. Pharmacotherapy includes disease-modifying therapies (DMTs), which aim to reduce relapse frequency, inflammatory disease activity, new MRI lesions, and disability progression. Available DMTs include interferon- β , glatiramer acetate, dimethyl fumarate, teriflunomide, fingolimod and other sphingosine-1-phosphate receptor modulators, cladribine, natalizumab, alemtuzumab, and B-cell-directed therapies such as ocrelizumab and ofatumumab. Symptomatic pharmacological treatment is additionally used according to individual patient needs. Current evidence indicates that no single intervention is sufficient for all aspects of MS; therefore, combining pharmacological treatment with appropriate lifestyle modification and rehabilitation can provide a more holistic approach to disease management. Such an integrated strategy may improve functional independence, symptom control, treatment outcomes, and overall quality of life in people living with MS. Further high-quality research is needed to establish optimal individualized and multidisciplinary

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management strategies across different MS phenotypes and stages of disease.

INTRODUCTION

Multiple sclerosis (MS) is a chronic, immune-mediated neurological disorder of the central nervous system characterized by inflammation, demyelination, axonal injury and neurodegeneration. It commonly affects young and middle-aged adults and may involve the brain, spinal cord and optic pathways. The clinical manifestations are highly variable and may include visual disturbances, sensory abnormalities, muscle weakness, spasticity, impaired coordination and balance, gait difficulties, pain, fatigue, cognitive dysfunction and psychological disturbances. The progressive accumulation of neurological impairment can substantially affect activities of daily living, social participation, employment and health-related quality of life. {2,4}

The management of MS has evolved from a predominantly pharmacological approach toward a more comprehensive and individualized model of care. Although advances in disease-modifying therapies (DMTs) have significantly improved the control of inflammatory disease activity by reducing relapses and new lesion formation and by delaying disability progression in appropriate patients, pharmacotherapy alone cannot adequately address all persistent symptoms and functional limitations. Consequently, optimal MS management requires integration of pharmacological treatment with lifestyle modification, rehabilitation, symptom management and regular multidisciplinary follow-up.

Lifestyle modification is an important component of comprehensive MS care. Regular physical activity and structured exercise can contribute to improvements in muscle strength, balance,

walking ability, physical fitness, fatigue and quality of life. Current evidence supports encouraging people with MS to participate in exercise and lifestyle physical activity according to their abilities, preferences, disability level and safety requirements. Exercise programmes may include aerobic activities, resistance training, flexibility exercises, balance training, walking, swimming or cycling. A gradual and individualized approach is particularly important in patients with significant disability or fluctuating symptoms.

Other lifestyle factors may also influence wellbeing and long-term disease management. A balanced diet, adequate nutrition, appropriate body weight, smoking cessation, sufficient sleep, stress management and appropriate self-management strategies may contribute to overall health and quality of life. Lifestyle interventions should not be considered substitutes for disease-modifying treatment, but rather complementary measures that support physical and psychological wellbeing and may help patients manage persistent symptoms. Studies of lifestyle self-management interventions have reported improvements in several quality-of-life domains, including physical, mental and emotional wellbeing and fatigue.

Rehabilitation represents another fundamental component of MS management and aims to maintain or restore functional independence, minimize disability, prevent secondary complications and improve participation in daily life. Because MS produces diverse and changing neurological impairments, rehabilitation should be individualized and delivered through a multidisciplinary approach. Physiotherapy may address muscle weakness, gait impairment, balance problems, mobility limitations and fatigue, while occupational therapy can assist with activities of daily living, energy conservation,



environmental adaptation and the use of assistive devices. Cognitive rehabilitation may be useful for memory, attention and executive-function difficulties, while psychological, speech and swallowing interventions can be incorporated when clinically indicated.

Evidence indicates that structured rehabilitation and exercise-based interventions can improve important functional outcomes in people with MS. Multidisciplinary rehabilitation may improve activity and participation, while physical therapy and exercise can improve mobility, muscular strength, fatigue and quality of life. Recent evidence further supports beneficial effects of exercise on balance, walking ability, walking endurance, fatigue and quality of life. Therefore, rehabilitation should be considered an ongoing and individualized process rather than a single intervention provided only after substantial disability has developed.

Pharmacotherapy remains essential for controlling disease activity and managing MS-related symptoms. Disease-modifying therapies are used primarily to reduce inflammatory disease activity, prevent relapses and new central nervous system lesions, and delay accumulation of disability in appropriate patients. Available DMTs include injectable agents such as interferon beta and glatiramer acetate; oral therapies such as dimethyl fumarate, teriflunomide, fingolimod and cladribine; and monoclonal antibodies such as natalizumab, ocrelizumab, ofatumumab and alemtuzumab. Selection of therapy should be individualized according to MS phenotype, disease activity, disability, MRI findings, treatment efficacy, safety, comorbidities, reproductive considerations and patient preferences.

In addition to DMTs, pharmacological management may be required for acute relapses

and persistent symptoms such as spasticity, neuropathic pain, bladder dysfunction, depression, anxiety and other MS-associated complications. Symptom-directed treatment should be integrated with rehabilitation and non-pharmacological strategies to achieve optimal functional outcomes. Thus, pharmacotherapy addresses disease activity and specific symptoms, whereas lifestyle modification and rehabilitation help patients maintain physical function, independence and quality of life.

Overall, the contemporary management of MS should be viewed as a comprehensive, patient-centred and multidisciplinary approach combining lifestyle modification, rehabilitation and pharmacotherapy. The integration of regular physical activity, healthy lifestyle behaviours, individualized rehabilitation and appropriate disease-modifying and symptomatic treatment may provide broader benefits than any single intervention alone. Such an integrated approach is particularly important because MS is heterogeneous and its clinical manifestations and functional needs change throughout the disease course.

Lifestyle Modification and Rehabilitation in Multiple Sclerosis

Lifestyle modification and rehabilitation are integral components of comprehensive management of multiple sclerosis (MS). Although disease-modifying therapies primarily target inflammatory disease activity, lifestyle and rehabilitation interventions aim to improve physical functioning, reduce symptom burden, maintain independence and enhance health-related quality of life. Since MS is associated with considerable variability in symptoms and disability, these interventions should be individualized according to disease characteristics, functional status, symptoms, preferences and the



patient's overall health condition.
{3,7,8,14,15,16,17,18,32}

Lifestyle Modification

Lifestyle modification in MS includes regular physical activity, appropriate exercise, healthy nutrition, smoking cessation, adequate sleep, stress management and effective self-management strategies. These measures are intended to promote general health and support the management of MS-related symptoms.

Physical activity and exercise: Regular physical activity should be encouraged in individuals with MS. Exercise programmes may include aerobic training, resistance training, flexibility exercises, balance training, walking, cycling, swimming and combined exercise programmes. Evidence indicates that exercise can improve balance, walking ability, walking endurance, muscle strength, fatigue and quality of life. A 2024 systematic review and meta-analysis involving 40 studies found significant improvements in balance, mobility, walking endurance, fatigue and quality of life following exercise interventions. Exercise should be introduced gradually and adapted to the individual's disability level and tolerance. Assessment by a physiotherapist or another professional experienced in MS can help establish an appropriate individualized exercise programme.

Healthy diet and nutrition: A balanced diet should be encouraged to maintain adequate nutrition and overall health. Patients should be encouraged to consume a varied diet containing fruits, vegetables, whole grains, adequate protein and healthy fats while limiting excessive intake of highly processed foods, added sugars and unhealthy fats. Dietary interventions should complement, rather than replace, evidence-based pharmacological treatment.

Smoking cessation: Smoking cessation is an important lifestyle intervention because smoking is associated with poorer outcomes and increased disability progression in MS. Individuals with MS should therefore be encouraged and supported to stop smoking.

Stress management: Stress-management approaches such as relaxation techniques, mindfulness, breathing exercises, yoga and psychological interventions may be incorporated into comprehensive self-management programmes. These approaches may help individuals cope with fatigue, emotional difficulties and the psychological burden associated with living with a chronic neurological disease.

Sleep management: Adequate and regular sleep is important for maintaining physical and cognitive function. Sleep disturbances should be identified and managed, particularly when they contribute to fatigue or reduced daily functioning.

Self-management: Self-management programmes may include education about symptoms, physical activity, energy conservation, stress management and strategies for maintaining participation in daily activities. Recent evidence suggests that integrated lifestyle and rehabilitation programmes may improve several quality-of-life domains, including physical, mental and emotional wellbeing and fatigue. {3,5,6,34,22,31,}

Rehabilitation

Rehabilitation is a multidisciplinary process designed to maintain or improve functional ability, independence and participation in daily life. It should be initiated according to individual needs and continuously adjusted as MS symptoms and disability change. Contemporary rehabilitation approaches increasingly integrate physical,



cognitive, psychological and lifestyle components rather than focusing on a single impairment.

Physiotherapy: Physiotherapy is an important component of MS rehabilitation. It may include strengthening exercises, aerobic training, stretching, balance exercises, gait training, mobility training and exercises aimed at improving coordination. Physical therapeutic interventions have demonstrated benefits for mobility, muscular strength, fatigue and quality of life.

Occupational therapy: Occupational therapy focuses on improving independence in activities of daily living. It may include energy-conservation strategies, activity pacing, assessment of functional difficulties, modification of the home or workplace and appropriate use of assistive devices.

Cognitive rehabilitation: Cognitive rehabilitation may be considered for individuals experiencing difficulties with memory, attention, concentration, information processing or executive functioning. It may involve cognitive exercises, compensatory strategies, memory aids and structured routines.

Fatigue management: Fatigue is one of the most common and disabling symptoms of MS. Rehabilitation-based fatigue management may involve energy conservation, activity pacing, appropriate physical activity, sleep management and behavioural strategies. Multidisciplinary rehabilitation and fatigue-management programmes can be incorporated according to individual needs.

Balance and gait rehabilitation: Balance and gait training can help individuals with walking difficulties, impaired coordination and increased risk of falls. Interventions may include balance

exercises, gait training, strengthening, mobility practice and appropriate walking aids.

Psychological rehabilitation: Psychological support may be incorporated to address depression, anxiety, stress and adjustment difficulties. Cognitive behavioural approaches, counselling, mindfulness and other psychological strategies may be used when appropriate.

Speech and swallowing rehabilitation: Speech and language therapy may be required in individuals with dysarthria, communication difficulties or swallowing impairment. Early assessment is important when swallowing difficulties may affect nutrition or increase aspiration risk.

Integrated Lifestyle and Rehabilitation Approach

Current evidence supports a shift toward integrated rehabilitation programmes that combine physical exercise with lifestyle, cognitive, psychological and self-management components. Such multimodal programmes may address several domains of MS simultaneously, including physical function, fatigue, mood, cognition and quality of life. Recent evidence also indicates increasing use of digitally supported and home-based rehabilitation approaches, which may improve accessibility and facilitate long-term participation.

Therefore, lifestyle modification and rehabilitation should be considered complementary components of MS management rather than alternatives to pharmacotherapy. A patient-centred multidisciplinary approach that combines healthy lifestyle behaviours, individualized rehabilitation and appropriate pharmacological treatment can help control disease activity, manage symptoms,



preserve functional independence and improve quality of life. {7,9,10,12,13}

Pharmacotherapy in Multiple Sclerosis

Pharmacotherapy is an essential component of the comprehensive management of multiple sclerosis (MS). The primary objectives of pharmacological treatment are to reduce disease activity, prevent relapses, delay the accumulation of neurological disability, manage acute exacerbations and control persistent symptoms. Pharmacological management should be individualized according to the clinical phenotype of MS, disease activity, severity, MRI findings, comorbidities, safety considerations, treatment response and patient preferences. Current therapeutic strategies include disease-modifying therapies (DMTs), treatment of acute relapses and symptomatic pharmacotherapy. {17,18,19,20,21,22,42,35,33,}

1. Disease-Modifying Therapies

Disease-modifying therapies are the main pharmacological approach for controlling the inflammatory activity of MS. They primarily aim to reduce the frequency of relapses, development of new or active MRI lesions and, for appropriate patients, the risk of disability progression. The available DMTs differ in their mechanisms of action, routes of administration, efficacy, safety profiles and monitoring requirements. Recent reviews emphasize the importance of early and individualized treatment selection based on disease activity and patient-specific characteristics.

A. Injectable therapies

Interferon beta:

Interferon beta modifies immune responses and reduces inflammatory activity within the central nervous system. It is available in different

formulations and has been widely used in relapsing forms of MS. Common adverse effects include flu-like symptoms and injection-site reactions. Laboratory monitoring may be required during treatment.

Glatiramer acetate:

Glatiramer acetate is an immunomodulatory agent that alters T-cell responses and reduces inflammatory activity. It is primarily used in relapsing forms of MS. Injection-site reactions are among the commonly reported adverse effects.

B. Oral therapies

Dimethyl fumarate:

Dimethyl fumarate has immunomodulatory and cytoprotective effects and is used in relapsing forms of MS. Important adverse effects may include flushing, gastrointestinal symptoms and lymphopenia. Appropriate blood-count monitoring is required.

Teriflunomide:

Teriflunomide inhibits dihydroorotate dehydrogenase, thereby reducing proliferation of activated lymphocytes. It is used for relapsing forms of MS. Hepatotoxicity, gastrointestinal effects and hair thinning may occur, and liver function should be monitored.

Fingolimod:

Fingolimod is a sphingosine-1-phosphate receptor modulator that limits lymphocyte migration from lymphoid tissues into the circulation and subsequently reduces lymphocyte entry into the central nervous system. It is used for active relapsing MS. Monitoring may be required for cardiac effects, infections, liver function and macular changes.



Cladribine:

Cladribine is an immune-reconstitution therapy that produces selective depletion of lymphocytes. It is used in selected patients with active relapsing MS. Because it can cause lymphopenia and increase susceptibility to infection, appropriate monitoring is necessary.

C. Monoclonal antibody therapies

Natalizumab:

Natalizumab is a monoclonal antibody that inhibits leukocyte migration across the blood–brain barrier by targeting $\alpha 4$ -integrin. It is highly effective in reducing inflammatory disease activity in relapsing MS. A major safety consideration is the risk of progressive multifocal leukoencephalopathy (PML), particularly in patients with relevant risk factors.

Ocrelizumab:

Ocrelizumab is a humanized monoclonal antibody directed against CD20-positive B cells. It reduces B-cell-mediated immune activity and is used in relapsing MS and, importantly, is also an approved disease-modifying treatment for primary progressive MS in appropriate patients. Infusion-related reactions and infections are important safety considerations.

Ofatumumab:

Ofatumumab is a fully human anti-CD20 monoclonal antibody that produces B-cell depletion. It is administered subcutaneously and is used for relapsing forms of MS. Injection-related reactions and infections may occur, and monitoring is required according to clinical circumstances.

Alemtuzumab:

Alemtuzumab targets CD52 and causes profound depletion of circulating lymphocytes, followed by immune reconstitution. It may be considered in selected patients with highly active disease when other therapies are inadequate or unsuitable. Because of potentially serious autoimmune, hematological and renal adverse effects, extensive monitoring is required.

2. Pharmacotherapy in Progressive Multiple Sclerosis

The pharmacological management of progressive MS is more challenging because neurodegenerative mechanisms become increasingly important as the disease progresses. Some DMTs have demonstrated benefits in selected progressive MS populations. Evidence from a 2024 systematic review and network meta-analysis suggests that ocrelizumab, siponimod and interferon beta-1b may have beneficial effects on disease progression in particular progressive MS populations, while treatment selection should remain individualized.

3. Treatment of Acute Relapses

Acute MS relapses are generally treated with high-dose corticosteroids when the relapse is clinically significant and treatment is appropriate. Methylprednisolone is commonly used to shorten the duration and severity of relapse symptoms and accelerate recovery.

Corticosteroids primarily reduce acute inflammatory activity and facilitate recovery from a relapse; they do not replace long-term disease-modifying therapy. Patients with severe relapses that do not adequately respond to corticosteroids may require specialist assessment for additional treatments such as plasma exchange.

4. Symptomatic Pharmacotherapy



MS produces a wide range of symptoms that may persist despite adequate disease-modifying treatment. Therefore, symptomatic pharmacotherapy is an important component of comprehensive care. Treatment should be selected according to the patient's specific symptoms, functional limitations and comorbidities. Recent pharmacotherapy reviews particularly emphasize management of pain, fatigue, spasticity and urinary dysfunction.eg,

Spasticity: Baclofen, tizanidine; other treatments may be considered according to severity

Neuropathic pain: Gabapentin, pregabalin, selected antidepressants

Fatigue: Amantadine and selected wake-promoting/stimulant therapies in appropriate patients

Bladder dysfunction: Antimuscarinic drugs; β 3-adrenergic agonists in appropriate patients

Depression/anxiety: Antidepressants such as SSRIs/SNRIs when clinically indicated

Constipation: Dietary measures plus laxatives or stool-softening agents when required.

5. Role of pharmacotherapy in comprehensive MS management

Pharmacotherapy should not be considered separately from lifestyle modification and rehabilitation. DMTs primarily target disease activity, while rehabilitation helps maintain mobility, independence, cognition, and functional ability. Lifestyle measures such as regular physical activity, healthy nutrition, adequate sleep, stress management, and smoking cessation can complement medical treatment. A multidisciplinary approach is therefore important

for improving functional outcomes and quality of life.

CONCLUSION

Multiple sclerosis is a chronic and complex neurological disorder that requires a comprehensive and individualized approach to management. Lifestyle modification, rehabilitation and pharmacotherapy are complementary components of effective MS care. Regular physical activity, appropriate exercise, healthy nutrition, smoking cessation, adequate sleep and stress management can support general health, improve physical function and contribute to better quality of life. Rehabilitation, including physiotherapy, occupational therapy, cognitive rehabilitation, psychological support and appropriate assistive interventions, helps manage disability, maintain functional independence and promote participation in daily activities.

Pharmacotherapy remains essential for controlling disease activity, reducing relapses and delaying disability progression through disease-modifying therapies, while corticosteroids and symptomatic medicines are used for acute relapses and MS-related symptoms. However, pharmacotherapy alone cannot address the complete physical, cognitive, psychological and functional burden of MS. Therefore, an integrated, patient-centred and multidisciplinary approach combining lifestyle modification, rehabilitation and appropriate pharmacotherapy is essential. Individualized treatment and regular monitoring can optimize therapeutic outcomes, improve functional independence and enhance the overall quality of life of people living with multiple sclerosis. {30,31,32,34,35,36,37,38,46,47,49,50}

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