



REVIEW

The role of rehabilitation in multiple sclerosis—is it worth it?

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Abstract

Introduction: Multiple Sclerosis (MS) is a complex immune-mediated disease that causes demyelination and degeneration within the brain and spinal cord. This may result in muscle weakness, abnormal tone, visual disturbances, decreased sensation, tremor/ataxia, bladder, bowel and sexual dysfunction, fatigue and impaired ambulation. Those symptoms cause disability and have a huge impact on quality of life (QoL).

Methods: Literature review about the evidence assessing the rehabilitation interventions for maintaining functional capacity and reducing risk of losing important abilities and independence. Databases of Cochrane Library/Pubmed/Medline were searched, from 2004-2016 with the keywords "Physical therapy", "rehabilitation", "multiple sclerosis", "review".

Results and Discussion: Physical exercise is safe and should be encouraged. Even though rehabilitation has no direct influence on disease progression, studies have shown that this intervention reduces the limitations, and helps to maintain QoL. Timing and setting of rehabilitation interventions should be selected individually. Benefits are generally higher in earlier phases of MS. A multidisciplinary approach, is the basic concept of any rehabilitation program. The main impairments that need to be specifically managed are spasticity, cognitive impairment, motor, sensory and visual deficits, fatigue and bladder/bowel dysfunction. Ambulation difficulties should be addressed to improve efficacy, efficiency and to reduce falls. Compensation through appropriate prescription of assistive devices, bracing, and/or wheelchairs will help improve safety. Cognitive training can improve memory span, working memory and immediate visual memory. New promising rehabilitation techniques may also be useful: impairment-oriented training, electromyogram-triggered neuromuscular stimulation, and robotic interactive therapies.

Conclusion: Rehabilitation has significant impact on achieving and maintaining QoL as well as on improving independence in patients with MS. A multidisciplinary and multimodal approach is the recommended model for neurorehabilitation interventions.

Keywords: Multiple sclerosis, Rehabilitation, Physical therapy, Quality of Life.

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Introduction

Multiple sclerosis (MS) is an immune-mediated inflammatory progressive disease of the central nervous system (CNS) [1]. It is the most common disabling neurological disease in young adults in Western Europe [2]. In most cases the disease has an unpredictable course, with recurring attacks of acute focal neurological deficits alternating with periods of remission [3].

The large range of symptoms include visual disturbances, ataxia, neuropathic pain acute paroxysmal pain, dysesthetic pain, weakness, coordination difficulties, impairment of walking, bladder and bowel disturbances, respiratory complications, weakness of the ventilatory muscles and may lead to a continuing decline in neurologic status and quality of life [1].

MS is an incurable disease and its pharmacological management relies upon three categories of substances, disease modifying drugs, corticosteroids for acute exacerbations and some drugs for symptomatic control [4].

There is a growing body of literature investigating the benefits of rehabilitation programs. There is also evidence suggesting that physical activity is not only safe and well tolerated for persons with MS, but additionally may be of value in alleviating some symptoms, preventing complications and possibly being neuroprotective.

Various studies suggest that exercise therapy can be beneficial in MS, with positive effects on fatigue, health-related quality of life and on muscle strength, in cases with mild to moderate disability.

Physical therapy has also a positive effect on balance and mobility. However, when the level of disability increases, the efficacy of physical therapy is less compelling [5,6].

To investigate the role of rehabilitation, the authors reviewed studies and randomised controlled trials indexed between January 2004 and February 2016.

Methods

In January 2016 a search was conducted of the following electronic databases: the Cochrane Library, Pubmed, Web of Science Core Collections, Library and Medline. The electronic databases were searched for studies indexed between January 2004 and February 2016. Individual search strategies were made up of keywords "Multiple Sclerosis, Rehabilitation, physical therapy".

Reference lists of relevant articles were also searched. To be included in the review, articles had to be published in English, include solely participants with MS, evaluate a physiotherapy intervention or an intervention containing a physiotherapy element. Articles were excluded if they were conference abstracts, or posters.

Articles were initially screened by title and abstract. Full articles were then read. Disagreements between the reviewers were resolved by consensus. There were 13 studies included in the review, 5 studies investigated phys-

iotherapy as part of a multidimensional intervention and 8 studies investigated the use of physiotherapy as a stand alone intervention.

Results

The Pubmed search resulted in a total of 160 papers. After the screening of titles and abstracts, 30 papers were considered to be eligible to be included, and after reading the full text, 15 papers were included in this review.

Discussion

Rehabilitation in MS should address the issues of body structure/body functions, activities and participation. A comprehensive assessment of functional disturbances, personal needs and expectations is essential for an individualized goal oriented rehabilitation program.

Rehabilitation should begin as soon as the patient develops some disability and should be divided into three main settings: Hospital Setting, Outpatient Setting and Home Setting.

Rehabilitation should be undertaken by a multidisciplinary team (MDT). The MDT should be headed by the physical medicine and rehabilitation physician. Each team member contributes to the success of the rehabilitation program.

Other team members include the physiotherapist in order to improve muscle strength, respiratory function, motor control, balance and gait, an occupational therapist for evaluation and training of patient's activity and participation abilities, a speech and language therapist who addresses swallowing difficulties and improves communication skills, a psychiatrist and a psychologist who impart counselling and teach strategies to cope with affective and cognitive impairment, a neuro-urologist who deals with bladder, bowel and sexual dysfunctions and a social worker, who contributes to resource management as well as social/family and labour integration. The MDT coordinate with each other, with family members and the patient in order to prioritize goals and interventions.

Studies have demonstrated the efficacy of a 6-week multidisciplinary rehabilitation program for patients with progressive MS and found improvements in disability, depression, fatigue, social experience and quality of life [6,7].

Exercise therapy

Evidence suggested that exercise therapy may actually impact disease course in persons at risk for MS and after the disease develops, it might be potentially considered as a disease modifying therapy [5]. Nevertheless, the evidence is inconclusive regarding the efficacy of using exercise therapy for the rehabilitation of people with progressive MS.

A recent review of 26 randomized controlled trials, of exercise in persons with MS found slightly decreased risk of relapse in the exercise group versus control (6.3% vs 4.6%) [8].

Briken et al. reported significant improvements in mobility, depression, fatigue, and cognitive function, and Miller et al. reported significant improvements in muscle strength and anxiety [6,7].

Deficits such as gait ataxia and limb incoordination are difficult to treat. Maintaining postural control is an important outcome. Gait can be improved by artificial support appliances like ankle foot orthoses, crutches and canes. Wheelchairs of various types can also be prescribed in order to prevent falls and injuries.

McCullagh et al. did a pilot study about the effects of a 12-week physiotherapy programme in seventy-six MS patients. The program included exercises such as treadmill walking, training, cycling, arm-strengthening exercises and outdoor walking. Follow up was carried out at months 3 and 6 after study initiation. The Modified Fatigue Impact Scale score significantly improved when compared to control, both after 3 and 6 months of training [9].

The use of a standing frame produced significant improvements in passive hip and ankle range of motion and a trend toward improvement in ankle spasticity [1,5].

Recently the use of robots like the Lokomat® and partial body weight bearing treadmill, has also been used at advanced rehabilitation centres [1,10].

Programs such as Yoga, aquatics and Tai Chi may help balance control and maintaining gait. Drugs have little role in this disability [1] (Table 1).

Functional Electrical Stimulation (FES)

The evidence is conflicting: few studies found positive results for an orthotic effect and decreased falls with FES in comparison with a home exercise plan.

Taylor et al. (Table 1), suggested that FES of the dorsiflexors is a well-accepted intervention that enables clinically meaningful changes in walking speed, resulting in a therapeutic effect in gait quality [11-13].

Pain management and Acupuncture

Pain is a common symptom in MS. Carbamazepine, gabapentin and pregabalin are commonly used for acute paroxysmal pain. Amitriptyline is useful for dysesthetic pain. Non-steroidal anti-inflammatory drugs and transcutaneous electrical nerve stimulation can also be tried [1].

Only 1 study investigated Chinese medical acupuncture in comparison with minimal acupuncture. The evidence is inconclusive for the rehabilitation of people with MS. Minimal acupuncture produced improvements in the psychological subscore of the Multiple Sclerosis Impact Scale compared with Chinese medical Acupuncture [1,14].

Inspiratory muscle training

Respiratory muscle weakness may contribute to ineffective coughing, pneumonia and sometimes acute ventilatory failure. When respiratory motor pathways are involved, respiratory muscle weakness produces a restrictive ventilatory defect. Respiratory complications are common in

terminal stages of MS and contribute to mortality in MS patients. Recent studies suggest that respiratory muscles can be trained for strength and endurance in MS patients.

There is evidence regarding the efficacy of using inspiratory muscle training for patients with MS. A significant improvement was found in maximal inspiratory pressure and maximal expiratory pressure in those using the inspiratory muscle trainer [6].

Botulinum Toxin A (BTX-A) injection and systemic pharmacotherapy

Spasticity can be generalised or focal. In MS it occurs due to demyelinating lesions in the brain and/or spinal cord, affecting the pyramidal tract. Spasticity can cause severe pain, disability, muscle fibrosis, sarcopenia and joint deformities. The restricted mobility can lead to increased limitation, isolation and depression. It is important to ascertain and neutralize any precipitating or aggravating factors. Those factors, the severity and the number of segments affected, the needs and expectations of the patient, the resources at hand and the experience of the MDT, will determine the intervention plan for spasticity management.

Focal spasticity in upper and lower limbs can be effectively treated by the use of BTX-A. There is good evidence regarding the efficacy of using a combination of BTX-A injections and manual stretches (Table 1).

Significant improvements were found in subjective relief of symptoms, fatigue, and functionality in activities of daily living in those who received a combination of BTX-A injections and manual stretches. However improvements were not maintained at 18 weeks post-intervention compared with 6 weeks post-intervention. Interventions incorporating segmental muscle vibration also produced significant improvements in spasticity, and those were maintained at 22 weeks follow-up assessments [15,16].

Generalised spasticity can be treated by the use of systemic drugs such as baclofen and tizanidine. Unfortunately, spasticity drugs can be associated with undesirable side effects like sedation, reduced cognition and limb weakness [1].

In rare cases, when spasticity is refractory to standard spasticity drugs, nerve block or sectioning nerves to specific muscles can be used. Likewise intrathecal baclofen pumps can be considered for cases of refractory severe generalized spasticity.

Compensatory strategies/ Educational treatment

Cognitive deficits occur in 60% of patients with MS. Mini mental state test, IQ tests and others can be used to detect deficits. Compensatory strategies such as appropriate time management, improved sleep, medication adjustment, memory calendars are helpful. Modafinil and CNS stimulants may be also helpful. Recently, immunomodulating therapies have been shown to improve cognition in some clinical trials [1].

Most patients complain of fatigue and the cause can be

Table 1. Studies Review regarding the efficacy of using exercise therapy for the rehabilitation of people with MS.

Study	Characteristics	Intervention	Results
Taylor et al. (2014) RT	n=25 Type of MS: primary or secondary progressive	Exercise group: peroneal FES (weeks 1 and 6), addition of gluteal FES (weeks 7 and 12), 8 sessions of core stability physiotherapy and HEP of core stability exercises (weeks 13 and 18), continue with HEP (weeks 19 and 24). FES wear continued for 12 week Control group: standard care with physiotherapy and HEP first followed by Follow up: 6, 12, 18 and 24 week Intervention duration: 24 weeks	Between groups: Observational gait analysis without FES (week 24) (P=0.044), with FES (week 18) (P=0.028) Group control: 10-m walk speed with FES (p<0.05), MSIS-29 phys week 24 (p<0.05), falls frequency (p<0.05)
Paoloni et al. (2013) RT	n=42 Type of MS: primary or secondary progressive	Exercise group 1 (G1): 60min passive movements to prevent contractions plus 30min segmental muscle vibration Exercise group 2 (G2): BTX-A injection 2wk before study then same as G1 Exercise group 3 (G3): BTX-A injection 2wk before study and 60min passive movements same as G1 Control group: not applicable Frequency: three time a week Follow up: 0, 10 and 22 week	Within G1: Knee MAS (P<0.001), ankle MAS (P<0.001), FSS (P=0.004) G2: Knee MAS (P<0.001), ankle MAS (P<0.001), FSS (P=0.05) G3: Knee MAS (P<0.001), ankle MAS (P<0.001) Both knee and ankle MAS higher at 22wk than 10wk (P<0.05), FSS (P=0.02), Barthel Index (P=0.004)
Dodd et al. (2011)	n=76 Type of MS: Relapsing-remitting	Exercise group: Progressive resistance training (leg press (LP), knee extension, calf raise, leg curls, reverse leg press) Control group: standard care plus attention social programme Session duration: 45 min. Frequency: twice a week Follow up: 10 and 22 week Intervention duration: 10 weeks	Exercise group improved significantly MFIS total and physical (p<0.05) compared to control group (week 10) for LP; RLP; RLPE; MFIS total and MFIS physical; and RLPE (week 22)
Miller et al. (2011) RCT	n=30 Type of MS: primary or secondary progressive	Exercise group: upper and lower limb strengthening task specific programme included upper and lower limb strengthening using theraband, mobile pedals, and weights. Control group: standard care Session duration: 60 min. Frequency: twice a week Follow up: 8 and 16 week Intervention duration: 8 weeks	Exercise group improved over time when compared to control group for right knee extension (p=0.018) and right knee flexion (p<0.001), left knee flexion (p=0.006)
Donnellan and Shanley (2008) RCT	n=14 Type of MS: primary or secondary progressive	Exercise group: Chinese medical acupuncture Frequency: twice a week Intervention duration: 5 weeks Follow up: 0 and 5 week	Exercise group improved when compared to control group for MSIS-29 psych subscore (p=0.04)
McCullagh et al. (2008)	n=30 Type of MS: Relapsing-remitting	Exercise group: Exercises: warm-up, exercise: treadmill, walking/running, cycling, armstrengthening, outdoor walking and cooldown Control group: standard care Session duration: 45 min. Frequency: twice weekly Follow up: month 3 and 6 Intervention duration: 3 months	Exercise group improved significantly MFIS (p<0.05) compared to control group (3 month)
Romberg et al. (2005)	n=114 Type of MS: diagnosis according to Poser	Exercise group: resistance combined with aerobic training- Resistance training included exercises for lower and upper extremities (theraband), and for the trunk; aerobic training included aquatic training Control group: standard care Session duration: not reported Frequency: W1-W3 resistance training session, 5 aerobic training sessions; W4-26 strength training 3 weekly and aerobic training once weekly; W21-W26 an extra strength training session per week was added Follow up: month 6 Intervention duration: 22 weeks	Exercise group improved significantly when compared to control group for 7.6 m Walking test (WT) (p=0.04); 500 m WT (p=0.008); first 50 m of the 500 MWT (p=0.006)
Surakka et al. (2004)	n=114 Type of MS: diagnosis according to Poser	<u>Exercise group:</u> Resistance training combined with aerobic training, warm up and scapular adduction, hip extension, arm pull down, seated abdomen, hip abduction, triceps push, leg curl, biceps brachii curl and knee extension; aerobic training included warm up, gymnastic exercises in shoulder-deep water and cool down <u>Control group:</u> standard care Session duration: the aerobic training lasted 30-40 min, the duration of the resistance training sessions was not specified Frequency: 5 resistance sessions and 5 exercise sessions over 3 weeks; 4 sessions during weeks 1-17 and 5 m sessions during the last 6 weeks Follow up: week 26 Intervention duration: 26 weeks	Exercise group improved significantly when compared to control for <i>Fatigue Index</i> for leg flexion in women (95% CI)

Table 1. Studies Review regarding the efficacy of using exercise therapy for the rehabilitation of people with MS. (cont.)

Study	Characteristics	Intervention	Results
Oken et al. (2004)	n=69 Type of MS: diagnosis according to McDonald criteria	<u>Exercise group 1:</u> aerobic training (bicycling or dual action stationary bicycles) <u>Exercise group 2:</u> yoga class <u>Control group:</u> wait list Session duration: 90 min for yoga session and variable duration for aerobic exercise Frequency: once a week Follow up: month 6 Intervention duration: 6 months	Exercise group 1,2 improved significantly when compared to control for energy and fatigue of the SF-36 health Survey (p<0.001), MFIS physical (p<0.01)

Adapted, with publisher permission, from "Sá M. Exercise therapy and multiple sclerosis" [4].

Abbreviations: BTX-A - Botulinum Toxin A; HEP - Home exercise plan; FES: functional electrical stimulation; FSS - Fatigue Severity Scale; LP - leg press; MAS - Modified Ashworth Scale MFIS - Multidimensional fatigue inventory score; MFIS total - multidimensional fatigue inventory total; MFIS physical - multidimensional fatigue inventory physical; MSIS-29 - Multiple Sclerosis Impact Scale; SF 36 short form 36 health survey; RCT - Randomized controlled trial; RLP - reverse leg press; RLPE - reverse leg press endurance (repetitions); RT - Randomized trial;

multifactorial. Fatigue management requires behaviour modification. Patients need to be trained to simplify work and use energy conservation strategies. Several medications like amantadine, modafinil, acetyl L-carnitine, methylphenidate have also been tried.

Speech and swallowing difficulties are due to spasm or stiffness of the muscles, poor motor control or muscle weakness. The patient is taught various exercises to relax and strengthen the muscles controlling the vocal cords and to coordinate movements of lips, jaw and tongue for chewing, word articulation and pronunciation. Changing the head or body position during eating may also help [1].

Bladder, bowel and sexual dysfunctions

Simple pelvic floor exercises should be taught for bladder disturbance. Self-catheterisation may be needed in some cases. Anti-cholinergic drugs are usually used to address the incomplete emptying and hyperreflexia.

Bowel dysfunction can be managed by establishing a bowel programme. Increase dietary fibre, liquid intake and use of laxatives for severe constipation.

For sexual dysfunction Tadalafil and Sildenafil represent the major breakthrough in the management of male sexual (erectile) dysfunction [1].

Limitations

The results may not be generalizable to all MS patients.

Implications for clinical practice

Despite the limitations presented, the results of this review suggested that rehabilitation programs may have a beneficial effect on patients with MS.

No relevant adverse events have been reported by most studies. Exercise therapy should be recommended for the rehabilitation of MS patients.

Conclusion

MS affects individuals in the prime of their lives and can be devastating for the patient, the entire family and so-

ciety. Increased public awareness and patient empowerment are mandatory.

Even though rehabilitation appears to have no direct influence on disease progression, the evidence presented is positive regarding the efficacy of physiotherapy for the rehabilitation of people with MS, improving personal activities and ability to participate in social activities, however, the evidence is generally weak because of the diversity in interventions and a lack of power within studies.

A multidisciplinary team approach is the recommended model for neurorehabilitation in MS. The rehabilitation program should be adapted, depending on the individual patient's needs and expectations, the surrounding environment, the severity and type of disability and, more importantly, the agreed treatment goals at a given stage. Improvement may persist for some months beyond the rehabilitation program, as a result of reconditioning, adaptation and appropriate use of medical devices, medication, self exercise programs and social support at home.

Abbreviations

BTX-A: Botulinum Toxin A; CNS: Central nervous system; FES: Functional Electrical Stimulation; MDT: Multidisciplinary team; MS: Multiple sclerosis

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