

Novel Physiotherapy Approach for Multiple Sclerosis

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Abstract

Multiple sclerosis is a chronic, complex disease with a variety of clinical symptoms and affects mainly young and middle-aged people. Research and therapies are focused on the early phase of MS, especially relapsing-remitting MS (RRMS). There is the need for novel therapeutic strategies especially oriented towards neuroprotection in the chronic phase. Accumulating data outlines the beneficial role of physiotherapy in individuals with MS. A physiotherapy program improves muscle strength, balance, walking capacity and decreases spasticity, while also enhancing mood, cognitive function and reducing fatigue. Currently, neurorehabilitation programs are among the most popular therapies for reducing the disabilities and social disadvantages of MS patients. Rehabilitation strategies in MS should be based on the promotion of motor learning-related neuroplasticity improving functional outcomes. Therefore, the interdisciplinary team is essential for maximizing the patient's ability to function.

In this review current treatment, symptoms and clinical phenotypes, the role of rehabilitation, main measures that are recommended to estimate disability, impairment and handicap of MS are presented. Additionally, aerobic training as a factor enhances cognitive function by upregulation of neurotrophins, such as brain-derived neurotrophic factor (BDNF) was showed. First of all this review focuses on the novel methods used in multiple sclerosis patients including telerehabilitation and cryostimulation.

Keywords: Multiple sclerosis; Physiotherapy; Aerobic training; Cryostimulation; Rehabilitation

Introduction

Multiple sclerosis (MS) is a multifactorial disease characterized by different pathophysiological processes such as inflammation, demyelination, oxidative stress, axonal damage and repair mechanisms. The participation of these processes is individual in patient's population [1-4]. There are four main types of MS, defined as: relapsing-remitting (RR), secondary progressive (SP) and primary-progressive (PP) and progressive-relapsing (PR) [1]. Approximately 80% of MS individuals have RRMS disease course characterized by relapse with neurologic symptoms such as paresis (mainly limbs), cognitive impairments, spasticity and others. About half of individuals with RR after 15-20 years of disease duration have constant progression with a wide range of symptoms (paralysis, ataxia, fatigue, spasticity and incontinence) and this stage is known as SP. MS patients with progression of clinical symptoms from the onset of the disease have PP (about 20%). Progressive forms of MS (SP; PP) are mostly dominated by axonal injury [2]. In contrast the RR phase is characterized by multifocal inflammation. Axonal loss is responsible for the transition from RRMS to progressive forms of the disease. MS has unpredictable onset and progression. The rate of disability progression is increased in patients with higher number of relapses during the first and second year of the disease [3]. A higher incidence of depressive symptoms and major depressive disorder in patients with MS is well documented and reported in both large community surveys and studies of persons with MS. Depressive symptoms in MS patients are also one of the important factors contributing to a lower quality of their lives [4].

Current therapies are mainly focused on the early phase of MS and they are most effective in reducing the number of relapses. There is the need for novel therapeutic strategies especially oriented towards neuroprotection in chronic phase and when immunomodulatory or immunosuppressive therapies are not effective [1,2,4].

Current MS Treatment

Research and therapies are focused on early phase MS, especially relapsing-remitting MS (RRMS). Current MS treatment is divided into first-line and second-line pharmacological treatment of RRMS. Disease-modifying drugs (DMD): interferon β (IFN β) (1b,1a) and Glatiramer acetate are standard therapy in first line treatment. The aim of using these drugs is to reduce the clinical relapse rate and their potential benefits in terms of disability progression are not so high but they do have good safety profiles. During the relapse corticosteroids are the most popular due to its anti-inflammatory effect [4]. Currently, a new generation of therapies constitute the second-line of treatment including Natalizumab, Mitoxantrone and the most recent Fingolimod (the first oral drug). These drugs are much more effective and are used in more severe non-IFN β -responder cases. However, they have a much higher level of risk of complications that are rare but very serious. The second-line therapies are much more effective than DMD but very expensive [2].

MS Rehabilitation

Historically, work out training was discouraged for MS patients due to the possibility of overheating the organism and increasing fatigue or triggering exacerbation. Currently, neurorehabilitation programs are among the most popular therapies in reducing the disabilities and

social disadvantages of MS patients [5]. Clinical studies have shown real benefits from exercises that are very effective in improving balance and increasing walking capacity. Moreover, special programs of work out based on aerobic training are very effective in reducing fatigue, enhancing mood and improving quality of life. Despite the demonstrated benefits, attrition in exercise intervention studies is a concern, ranging from just over 18.6% to 42.4%. A high-energy cost of walking, respiratory muscle dysfunction and deconditioning are the important factors contributing to low exercise tolerance in MS patients [6]. This situation buildup limitation of physical activity and may reduce the ability to participate in daily social and family activities [7]. One of the main aims of rehabilitation in MS is to maintain and improve functional independence. In particular, aerobic exercise seems to be a promising rehabilitative tool for patients with MS because it could positively affect both maximum exercise capacity [8].

Balance and postural control problems are present in 20% of patients with MS at onset and 80% in chronic cases [5]. Many studies show that balance disorders are the leading cause of falls for people with MS (between 52% and 63% from 2–6 months; increases with age and MS progression) [7]. The risk of falling significantly decreases the mobility and quality of life. The National MS Society in 1985 published the Minimum Record of Disability (MRD) [10]. This is the most widely used MS outcome measure. The MRD followed the World Health Organization (WHO) classifications for 3 types of MS dysfunctions (impairment; disability; handicap) that are the main fields of rehabilitation [11]. Impairment refers to clinical signs and symptoms of neurologic disease; Disability refers to the personal limitations caused directly on the activities of daily living by the neurologic impairment; Handicap refers to a reduced ability to participate in social and environmental situations due to the effects of the disability or impairment on the patient [9-12] (Figure 1).

The MRD includes the special scales to measure the 3 types of dysfunction in MS patients:

1. Impairment – Expanded Disability Status Scale (EDSS)

2. Disability - Incapacity Status Scale

3. Handicap - Environmental Status Scale

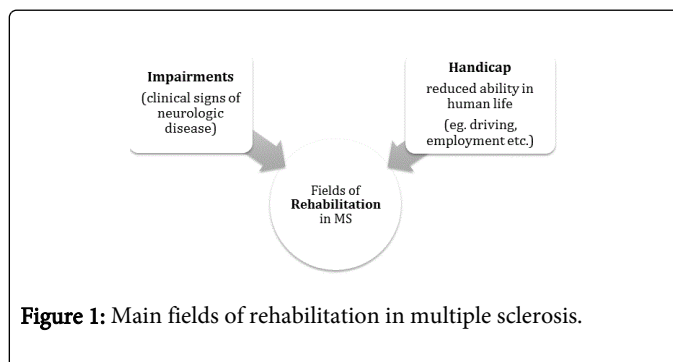


Figure 1: Main fields of rehabilitation in multiple sclerosis.

The most commonly used is the EDSS originally developed by Kurtzke in 1955 as the Disability Status Scale (DSS). The EDSS rated impairment due to MS on a 1 to 10 point scale. Subsequently, the scale was expanded to include half point steps. According to the EDSS score the patients were divided into the following subgroups: low physical disability (EDSS ≤ 3.5), moderate physical disability (3.5 < EDSS ≤ 6.5) and high physical disability (EDSS > 6.5). An advantage of the EDSS is that administration of it takes only 10 to 20 minutes and includes evaluation of all major areas of the CNS as they apply to MS. However, it is more heavily weighted toward effects on ambulation and provides limited assessment of upper extremity function, cognitive function and fatigue. Moreover, it does not detect change over a short period of time. EDSS scores are bi-modal, clustering at 3 to 4 and 6 to 7 [13].

The National MS Society Clinical Outcomes Assessment Task Force reviewed multiple measures to determine which were reliable, correlated well with disease duration, changed over time and had concurrent and predictive validity based on the EDSS [9].

Three measures of MS functional composite were recommended to estimate disability and impairment (Table 1).

Test	Measurement	Time to perform in minimally affected	Estimation of significant change	Limitation
The timed 25-foot walk	walk	3-5 seconds	Increase of more than 20%	
The nine-hole peg test and Paced Auditory Serial Addition	upper extremity function	18 to 20 seconds without impairment	20% decline in the score	severe upper extremity weakness or tremor
Test— 3-second version (PASAT-3)	Mild cognitive impairment (informational processing speed and attention)	15 to 20 minutes including practice trials	effect of treatment is reflected by a larger improvement on the test compared to the control group	significant practice effects over repeated measures

Table 1: The main measures of MS functional composite recommended to estimate disability and impairment

In mature form MS represent almost all neurological symptoms connected with persistent inflammatory state and multifocal injury of CNS. So, interdisciplinary team is essential for maximizing the patient's ability to function [4]. There are separate roles in the rehabilitation team; each member has its own specific area where he excels in knowledge and expertise. Members communicate with each other and with the patients, prioritizing and coordinating treatment regimens and goals. One of the more significant components in managing the disease is rehabilitation, which starts as early as the beginning of the disease. Prevention, diagnosis, long-term and acute

treatment - these are all parts of rehabilitation process, together with community integration, end-life management, and prevention of handicaps and hypokinesia.

Augmenting and maximizing life quality is a fundamental challenge of rehabilitation team. The team observes the significance of different understanding of quality of live among different patients, and recognizes its impact on patient function in both psychosocial and physical environments. As a result, rehabilitation team along with the patient aims to maximize and augment his or her ability to exist

independently both in the community and at home, addressing patient's concerns, as they appear, comprehensively [14-19].

Prevention is another fundamental element in rehabilitation. It includes wide variety of challenges, such as muscle contractures, prevention of falls and decubitus ulcers, but also includes prevention of loss of the employment and maximizing patient performance at the workplace. For best results and prolonged benefit, inpatient rehabilitation should be repeated periodically.

Therapies for some conditions, such as MS, are mostly concluded at outpatient setting or at home. One of the most frequently requested services is physical therapy, occupational therapy, which is followed by psychotherapy and massage therapy. Some patients also request the aid of social workers, and some request services of language and speech therapists [5].

Novel Therapies

Aerobic training enhances cognitive function

Rehabilitation complex strategies in MS should be based on promotion of motor learning-related neuroplasticity improving functional outcomes [20,21]. Aerobic exercise training not only improves mobility, balance, and motor function but also enhances cognitive function by upregulation of neurotrophins, such as brain-derived neurotrophic factor (BDNF).

BDNF is a neurotrophin involved in neuroprotection, neurogenesis, and neuroplasticity, and has been identified as a key mediator of motor learning and rehabilitation. Moreover, considerable evidence shows that exercise-induced increases in BDNF benefit cognitive function. However, systemic levels of BDNF are increased for approximately 10 to 60 minutes following a bout of aerobic exercise in humans [22]. A meta-analysis of 18 aerobic exercise training intervention studies in older adults concluded that the largest effects on cognition occur in the executive control domain, including functions such as planning, scheduling, working memory, and multitasking [23]. Gathered data proves positive influence on cognitive function and BDNF levels increase, training exercises should consist of: (1) sessions of aerobic exercises longer than 30 minutes [24], intensity of exercises 70% maximum heart rate [22], occurring 4 days a week [22] with both resistance and aerobic exercises combined [24]. High-intensity intervals and cycling [25] could be remarkably efficient when it comes to immediate benefit of acute aerobic training on cognitive function; nevertheless evidence also exists that only 30 minutes of aerobic training at 60% heart rate max. is very effective for patients with chronic disease and results in increase of BDNF levels. Present studies show that muscle oxidative capacity in patients with MS found a lowered maximal oxygen uptake, smaller type 1[26] skeletal muscle fiber diameter, lower succinate dehydrogenase activity, and complex 1 deficiency in skeletal muscle mitochondria, as opposed to healthy counterparts. This indicates a lowered muscle oxidative capacity in subjects with MS. Aerobic training in MS should be individually corrected.

Telerehabilitation

Nowadays telemedicine is very popular in many countries especially in rural areas where everyday transport is limited. In response to this situation, there are some rehabilitation services based on telerehabilitation (TR). Different platforms supporting online TR for

first of all patients with chronic neurological disorders with bulk of motor, functional and cognitive impairments. These platforms enable patient monitoring, either asynchronously through forums, e-mail, wikis, or blogs or synchronously through chat servers, instant messaging, videoconferencing, collaborative browsing, or remote presentation. Patient monitoring allows for the observation of progress of the therapy as well as modification or adjustment of an individual program based on planned and accomplished objectives. The key feature of this therapy is interaction and sensory feedback with patients via a highly motivating multitasking virtual environment based on virtual daily activities. Patients rank the intensity and difficulty of these tasks, thereby providing real-time information with regard to the achieved objectives [27]. Biofeedback is very useful for improving gait and balance; auditory or visual feedback during gait transiently improves gait parameters in patients with MS [28].

Cryostimulation

A relatively novel modality of cryotherapy is whole-body cryotherapy (WBC), which consists of short 2-3min. long exposure to extremely cold air (-100 to -120C) in a temperature- controlled chamber or cryocabin. Sessions of partial-body cryotherapy (PBC), in which the head is not exposed to cold, has also been used as a similar modality of WBC [29]. WBC and PBC session decreased skin temperature, however, WBC induced a greater decrease compared to PBC [29]. Cryostimulation in MS patients with neurological deficits has increased not only muscle strength, decreased spasticity and disability reduction in EDSS (Expanded Disability Status scale) but also higher level of antioxidative status has been observed. Treatment with cryostimulation caused significant increase of TAS level in plasma of depressive MS patients compared to untreated patients and reached the values of healthy controls. There are only a few data concerning treatment of MS patients with WBCT (110-160°C). However cooling (7-26°C) mainly heat-sensitive MS patients as a factor improving functional performance of MS patients was used [30]. In our previous studies we observed a statistically significant positive improvement in functional status of SPMS patients in EDSS estimations after 10 WBCT sessions [31].

Conclusions

Rehabilitation complex strategies in MS should be based on promotion of motor learning-related neuroplasticity improving functional outcomes. Existing therapeutic strategies in MS is to reduce the process of neuroinflammation, and most drugs registered to treat the disease has immunomodulating properties. According to current knowledge, it appears that rehabilitation strategies could constitute a valuable element supporting the traditionally used treatment. Aerobic training factor as well as cryostimulation is a potential positive impact on the neurobiological processes in the brain primarily on motor skills and cognitive abilities. In neurodegenerative diseases such as multiple sclerosis, there is an increased demand for neurotrophic factors affecting neuroplasticity and neuroprotection processes of the central nervous system (CNS) [32]. There is a need to focus research on novel methods of physiotherapy especially in chronic phase of MS.

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