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Rehabilitation in Secondary Progressive Multiple Sclerosis in Patients: Early Outcomes

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Abstract

Introduction: Multiple Sclerosis (MS) affects approximately 110,000 people in Italy and MS is a leading cause of disability in young adults. Rehabilitation interventions are frequently used as clinical strategies for improving or maintaining functional state.

Methods: We assessed 9 patients with secondary progressive multiple sclerosis (SP-MS): Four female and five male with a mean age of 47.3 years. The mean score EDSS was 7 (values from 3.5 to 8.5). All patients were hospitalized from eight to ten weeks; MSIS-29, EBN, Hamilton, FIM, Barthel, Tinetti and FSS tests were administered. All patients received one weekly spine manipulation in accordance with Palmer, Sutherland, Makenzie procedures both in supine and upright position. Three times a week the patients received also a draining massage of head and lower limbs by Muscular Acoustic Modulator (MAM) device. Eighty minutes a day, for 6 days a week, all patients had neuro-motor rehabilitation.

Results: Only some data from clinical tests showed statistically significant differences, before and after treatments. These data are: FSS scale: $p<0.01$ (H Kruskal-Wallis=6.7996 with degree of freedom=1); Memory test with deferred Prose: $p<0.05$ (H Kruskal-Wallis=4.7193 with degree of freedom=1); Memory test with immediate Prose: $p=0.0920$ Trend (H Kruskal-Wallis=2.8382 with degree of freedom=1).

Conclusion: In our study FIM, Bartel, Tinetti tests showed reductions in clinical disability without statistical significance. We had statistically significant differences, after 6 weeks by this innovative rehabilitation treatment both on the chronic fatigue on the cognitive status in inpatients with SP-MS. These preliminary positive results encourage us to continue research on a larger sample of patients.

Keywords: Rehabilitation; Multiple sclerosis; Venous compression syndrome; Sound vibration

Introduction

Multiple Sclerosis (MS) affects approximately 110,000 people in Italy and is a leading cause of disability in young adults. Rehabilitation interventions are frequently used clinical strategies for improving or maintaining functional status. To date the pharmacological therapeutic approaches are based on the need to put a stop to an immune system that attacks the myelin sheath, which covers the neuronal axons, creating lesions that, with the passage of time, can create irreversible damage.

In MS patients the brain and spinal cord eliminate drain deoxygenated blood and toxins with great difficulty [1]. This failure is due to reduced drain for narrowing of the cerebral veins and blocks that are found in the venous segments located outside the skull, especially in the neck, chest and abdomen. The reduced venous drainage has direct effects on the drainage of Cerebrospinal Fluid (CSF) surrounding the brain and spinal cord whose action is to protect them from trauma, feed them and drain toxic substances.

This cerebral spinal venous insufficiency can be diagnosed through a specific procedure EchoColorDoppler (ECD); which enables the identification of two types of venous blocks: The one inside the vein for valvular anomalies and the external one for compression of the veins caused by the surrounding tissue. The first one may benefit from endovascular treatment (angioplasty), the second by a rehabilitative physical therapy [2].

The anatomy and physiology until now denied the presence of brains, bone marrow, ear and eye, lymphatic drainage system which, therefore, would seem to be isolated organs from this point of view from the rest of the body. We hypothesize that sight, hearing and smell nerves are like compensatory expansion chambers in case of increased intracranial pressure. Russian studies Speransky and more recent Koh et al. instead reported experiments showing drainage from the CSF and brain interstitial system in both cervical and peripheral lymphatic system [3,4]. Our work 2001 showed the presence of an eye lymphatic drainage system. Recent publications of cochlea RM assessment have objectively shown the presence of a hydrops into the cochlea in Meniere's disease patients. The most current research has shown that not only the brain is equipped with its own lymphatic system, but also that such a system consists of two anatomically and functionally distinct parts [5]. A part of this system is a classic lymphatic system composed of true lymphatic vessels. The other, called gliolymphatic system is mainly built by astrocytes. These two brain draining systems

recently discovered, likely to play a substantial role in the pathogenesis of many neuro-immune diseases and neurodegenerative disorders such as multiple sclerosis, Parkinson's disease, and Alzheimer's disease Simka [6].

In 2011 we find the compression syndromes of the jugular and the vertebral veins and are given the indication for specific cervical adjustments of the first vertebrae with positive clinical results [7]. The aim of this procedures was to improve the venous brain drainage and consequently of the CSF. In 2013 starting from the rational that the CSF was correlated with lymphatic system, we treated by sound vibration tissue draining therapy (Dreno-MAM) with positive clinical effects, both MS patients with venous compression syndromes or intravenous blocks [8].

The aim of this pilot study was to evaluate the efficacy of physical rehabilitation treatments on inpatients with Secondary Progressive Multiple Sclerosis (SP-MS).

Methods

Sample

We assessed 9 patients with (SP-MS): four female and five male with a mean age of 47.3 years. The mean score EDSS was 7 (values from 3.5 to 8.5). All patients were hospitalized from eight to ten weeks. The ongoing pharmacological treatments were continued. Each patient provided a signed informed consent to participate to this study.

Measures

Multiple Sclerosis (MS) is a chronic and progressive disabling disease with multiple potential clinical intervention points during its course. It is therefore appropriate to have quality measures specific for this condition that span the course of the disease. International Organization of Multiple Sclerosis Rehabilitation Therapists (IOMSRT) says Evidence Based Medicine (EBM) is: "The conscientious, explicit, and judicious use of current best evidence in making decisions about the care of an individual patient."

Improving the quality of health care is essential in the practice of medicine. Fundamental to these efforts to improve quality is the ability to measure care because we cannot improve what we do not measure. These measures are intended to be used by stakeholders to quantify the quality of care provided to patients with MS. Disease-specific quality measures in physiatry provide a framework that can assist clinicians in practice measurement and modification; these have the potential to benefit both subspecialist and generalist alike. The World Health Organization's International Classification of Impairments, Disabilities and Handicap [9] were used as the conceptual basis for the choice of the best outcomes to be measured. Assessment of neurological status (impairment) was determined by Kurtzke's Functional System Scale (FSS) and Expanded Disability Status Scale (EDSS). This scale is composed of eight subscales, each measuring a specific function within the central nervous system. EDSS score lower than 4 addresses impairment, while grades 4 to 10 are strongly dependent on disability and particularly locomotion. Although some criticisms have been expressed on psychometric properties of this scale not be sufficiently sensitive, it has been used in most clinical trials [10].

Disability was assessed by the motor and the cognitive domains of the Functional Independence Measure (FIM). The underlying rationale for classifying an activity as "independent" or "dependent" is whether another person (a helper) is required and to what extent. There is a good evidence to support the reliability and validity of the FIM to assess disability. Scores were obtained from patient interview by a FIM trained physiatrist. In accordance with the guidelines, scores were consistently determined by actual performance of tasks on a daily basis, rather than each individual optimum performance.

In our study we assessed quality of life by the Multiple Sclerosis Impact Scale (MSIS-29) questionnaire [11]; depression by Hamilton Rating Scale for Depression (HRSD) [12]; cognitive status by Brief Neuropsychological Examination (ENB) questionnaire [13]; chronic fatigue by Fatigue Severity Scale (FSS) questionnaire [14], disability by Functional Independence Measure (FIM) scale [15], activities for daily living (ADLs) by Barthel Index [16] ; gait balance by Tinetti scale [17].

Before and after recovery period MSIS-29, ENB and Hamilton psychological tests, FIM, Barthel, Tinetti and FSS physiatric assessment tests were administered in all patients.

Rehabilitation Program

All patients received one weekly spine manipulation in accordance with Palmer, Sutherland and Makenzie procedures in four steps. In supine position: first step for the opening of foramen magnum; second step for the realignment of C1; third step for realignment of C2. In upright position: fourth step for realignment of other cervical vertebrae and cranial chiropractic adjustment. After manipulation procedure the patients received one acoustic vibration treatment by Muscular Acoustic Modulator (MAM) device on treated areas [18]. The patients received also a draining massage of head and lower limbs, three times a week, by MAM device. Eighty minutes a day, for 6 days a week the patients had individual neuro-motor rehabilitation. The individual neuro-motor rehabilitation consists in passive and active aided mobilizations, stretching of the four limbs and spine, reinforcement and strengthening muscles, motion coordination exercises, functional rehabilitation of gait and proprioceptive exercises.

Statistical Analysis

We used the parametric equivalent of the Kruskal-Wallis test to perform one-way Analysis of Variance (ANOVA) and for testing whether data before and after treatments originate from the same distribution. Kruskal-Wallis test indicates that at least one sample stochastically dominates one other sample. The test does not identify where this stochastic dominance occurs. Anyway, in our pilot study with a very little sample, the Kruskal-Wallis test is enough potent to reject the null hypothesis that the medians of all groups are equal; and the alternative hypothesis is that at least one median of one group is different from the median of the other group.

Results

Only some data from clinical tests showed statistically significant differences, before and after treatments. These data are: FSS scale: $p < 0.01$ (H Kruskal-Wallis=6.7996 with degree of freedom=1) (Table 1); Memory test with deferred Prose: $p < 0.05$ (H Kruskal-Wallis=4.7193 with degree of freedom=1) (Table 2); Memory test with immediate Prose: $p = 0.0920$ Trend (H Kruskal-Wallis=2.8382 with degree of freedom=1) (Table 3). FIM, Bartel and Tinetti tests show the reduction of some aspect of clinical disability but the total scores not were statistically significant.

Discussion

Historically, MS care focused on rehabilitation and symptomatic management; however, this focus broadened with the development of Disease-modifying Therapies (DMTs), resulting in pharmacologic

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Fatigue Severity Scale (FSS)
p<0.01 (H di Kruskal-Wallis=6,7996 with degree of freedom=1)

Visit	pt.	Σ	Mean	Variance	Std. Dev.
1	9	499,0000	55,4444	44,5278	6,6729
2	9	375,0000	41,6667	117,5000	10,8397

Visit	Minimum	25%	Median	75%	Maximum	Mode
1	45,0000	50,0000	54,0000	62,000	63,0000	50,0000
2	27,0000	32,0000	41,0000	49,0000	58,0000	27,0000

Table 1: Results of Fatigue Severity Scale (FSS).

Deferred prose memory test (MPD)
p<0.05 (H di Kruskal-Wallis=4,7193 with degree of freedom=1)

Visit	pt.	Σ	Mean	Variance	Std. Dev.
1	9	15,60,000	1,73,333	123,0000	47,958
2	9	19,70,000	2,18,889	I 9,1111	3,0185

Visit	Minimum	25%	Median	75%	Maximum	Mode
1	9,0000	14,0000	18,0000	20,0000	23,0000	18,0000
2	15,0000	21,0000	22,0000	24,0000	25,0000	22,0000

Table 2: Results of Brief Neuropsychological Examination (ENB).

Immediate prose memory test (MPI)
p=0.0920 TREND (H di Kruskal-Wallis=2,8382 with degree of freedom=1)

Visit	pt.	Σ	Mean	Variance	Std. Dev.
1	9	12,40,000	1,37,778	17,9444	4,2361
2	9	16,50,000	18,3333	25,5000 0498	5,0498

Visit	Minimum	25%	Median	75%	Maximum	Mode
1	7,0000	11,0000	14,0000	16,0000	21,0000	16,0000
2	10,0000	15,0000	19,0000	21,0000	25,0000	25,0000

Table 3: Results of immediate prose memory test (ENB).

treatments that effectively reduce relapses and potentially slow the progression of disability. Consequently, DMTs often dominate many discussions regarding MS care, regardless of the fact that they do not reverse disability or restore function, arguably the primary goal of those with MS. Comprehensive, multidisciplinary care goes beyond the management of DMTs in MS treatment plans and strives to improve patient outcomes, functionality, and quality of life, goals that will likely prove to hold considerable importance as health care reimbursement transitions from a fee-for-service to a value-based paradigm. It is therefore likely that achieving improvement in some of the outcomes delineated in the American Academy of Neurology's (AAN) quality measures for MS will necessitate involvement of rehabilitation specialists.

In 2015 the systematic review of the literature (1970–2013) and classified articles using American Academy of Neurology criteria highlights the paucity of well-designed studies, which are needed to evaluate the available MS rehabilitative therapies. Inpatient exercises (3 weeks) followed by home exercises (15 weeks) possibly is effective for improving disability. In the 2015 the Simka review summarises current knowledge on the lymphatic system of the brain. It has long been believed that the central nervous system is characterised by the lack of a lymphatic system and that the role of the lymphatic system is played by Cerebro-spinal Fluid (CSF). Recently, research has shown that not only is the brain equipped with its own unique lymphatic system, but also that this system consists of two anatomically and functionally distinct parts. One part of this system is a classic lymphatic system, i.e., the structure composed of genuine lymphatic vessels. The other, so-called glymphatic system is primarily built by astrocytes. The newly discovered lymphatic system of the brain is likely to play a substantial role in the pathogenesis of many neuro-immune and neurodegenerative disorders, such as: multiple sclerosis, Parkinson's disease, and Alzheimer's disease [6]. On the basis of this rational and of our previous experience, we used specific vertebral manipulations and applications total body tissue drainage by MAM device.

In 2016, Sandroff says in his Systematic, Evidence-Based Review of Exercise, Physical Activity, and Physical Fitness Effects on Cognition in Persons with Multiple Sclerosis: "Collectively, there is insufficient well-designed research to definitively conclude that exercise, physical activity, and physical fitness are effective for improving cognition in MS" [19].

The AAN systematic review could have, to a greater extent, highlighted the problems created by these methodologic issues and barriers to higher-level research in rehabilitation and argued for solutions that may ultimately influence funding agencies. The question is how to fulfill this need for well-designed trials in rehabilitation. Organizations such as the AAN, CMSC, and IOMSRT have a role in developing and disseminating clearly defined interventions, appropriate endpoints, and effective outcome measures. Collaboration with organizations specific to neurologic rehabilitation, such as the American Physical Therapy Association's Neurology Section, the American Occupational Therapy Association, and the American Speech-Language-Hearing Association, may help enhance and expand MS-specific rehabilitation research currently being performed by rehabilitation scientists and exercise physiologists. Standardized protocols and validated endpoints are needed for all larger studies, especially ones involving multiple centers. It is essential to formulate well-designed trials of rehabilitation therapies and techniques, and to overcome the major challenges of having a placebo group and blinding participants in rehabilitation studies. The need for well-designed research trials of rehabilitation in MS remains ongoing and imperative [20]. The last cited reviews prompted us to use, in our study, the most used questionnaires and physiatric tests. These tools have allowed us, even if in a small sample of patients, to detect positive results both on a cognitive that chronic fatigue impairments.

Conclusion

In our study FIM, Bartel, Tinetti tests showed reductions in clinical disability without statistical significance. We had statistically significant differences, after 6 weeks by this innovative rehabilitation treatment both on the chronic fatigue on the cognitive status in inpatients with SP-MS. These preliminary positive results encourage us to continue research on a larger sample of patients.

Disclosure

Non-financial relationship exists.

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