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ORIGINAL COMMUNICATION

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Effects of a short outpatient rehabilitation treatment on disability of multiple sclerosis patients

A randomised controlled trial

Abstract It is well known that neurorehabilitation can reduce disability or improve handicap of people with multiple sclerosis (MS). The aim of this study was to evaluate the effectiveness of a short period (6 weeks) of a tailored, individualised outpatient rehabilitation program in people with progressive MS. A randomised-controlled trial was undertaken in patients with primary and secondary progressive MS referred to the Centro Sclerosi Multipla of Catania. One hundred and eleven patients were assessed at baseline and at 12 weeks with validated measures of disability (Functional Independence Measure (FIM)) and impairment (Expanded Disability Status Scale (EDSS) and Functional Systems Scale). Of the 111, 58 were randomly assigned to the treatment group and 53 to the control group. All patients had been previously trained in a home exercise program. Both groups were well matched for age, sex, disease duration and severity, disability and quality of life (Short Form-36). At the end of 6 weeks patients allocated to the rehabilitation treatment group showed significant improvement in their level of disability compared with the control group, while the level of impairment did not change. Thirty-two patients of the treatment group and four of the control group improved on the FIM by two or more steps at 12 weeks ($p < 0.0001$). An improvement by 1 EDSS step occurred in only two patients of the treatment group and in one patient of the control group. Benefits were maintained for a further six weeks. This study demonstrates that a short outpatient rehabilitation treatment improves disability of MS patients, without changing their impairment and confirms the effectiveness of rehabilitation in people with MS.

Key words rehabilitation · outpatient · program · disability · FIM

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Introduction

Physical rehabilitation is commonly administered to multiple sclerosis (MS) patients, but little attention has been given to the development of effective rehabilitation strategies for such patients [31, 32]. That is probably due to the belief that the chronic progressive nature of MS makes the patients poor candidates for rehabilitation. However, a number of publications have described comprehensive care and neurorehabilitation in MS [1, 3, 4, 6,7, 9,14, 26, 29]. More recently several controlled studies have demonstrated the effectiveness of rehabilitation on disability and quality of life [12, 28]. In other studies it has been shown that rehabilitation can also improve the fitness of MS patients [24] and reduce their fatigability [8, 24]. Some studies were performed with an inpatient rehabilitation program [2, 12, 17, 28]. Others were carried out with an outpatient rehabilitation program [8, 24]. These studies raise the question of which is the most suitable approach to rehabilitation for MS patients. The aim of this study was to evaluate the effectiveness of a short outpatient rehabilitation treatment on disability of MS patients.

Methods

Patients

All consecutive MS patients referred to the Centro Sclerosi Multipla of the Policlinico of the University of Catania, between January 1998 and December 1998 were included in the study.

A total of 111 patients with clinically definite MS (Poser et al) [25] were enrolled and randomised over a one-year period. All patients had to have either primary or secondary progressive MS [20] and were felt to have the potential to benefit from rehabilitation. Each patient underwent a complete neurological examination. The specific criteria for enrolment for both outpatient rehabilitation (treatment group) and a home exercise program (control group) was an EDSS score ranging from 4.0 (at minimum, the disability was severe enough to preclude the ability of the patient to walk beyond 400 meters without assistance), to 8.0 (the patient was restricted to a bed or chair, but retained many self-care functions and had effective use of the arms) [19].

Exclusion criteria were as follows: one or more exacerbations in the preceding 3 months; cognitive impairment likely to interfere with adherence to the study, as determined by a Mini-Mental State Examination (MMSE) score of ≤ 24; history of cardiovascular, respiratory, orthopaedic, psychiatric, or other medical condition precluding participation; pregnancy; treatment with immunosuppressive therapy, interferon, copolymer, 4-aminopyridine, or experimental drugs in the six months before enrolment; rehabilitation in the three months before admission; non Italian speaking patients.

Randomisation into two groups was obtained in accordance with a computer-generated randomisation sequence by using consecutively numbered, opaque, sealed envelopes. Three physicians were the assessors during the study: the referring physician recorded patients' general information, clinical data and follow-up history. The treating physician was responsible for the rehabilitation program. The evaluating physician, who was blinded to treatment assignment, administered the evaluation scales which consisted of Kurtzke's EDSS with Functional System Scales (FSS) and Functional Independence Measure (FIM). Each patient assigned to one of the two rehabilitation programs by the treating physician (FP) was assessed by the evaluating physician (MRC) within 24 hours of admission and re-examined at weeks 6 and 12. The assessors had no access to the initial scores before the second and third assessments. Treating and evaluating physicians were not allowed to share information about the treatment. Separate and different clinical record forms were given to each physician.

Measures

The World Health Organisation's International Classification of Impairments, Disabilities and Handicap [36] was 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 EDSS [19]. This scale is composed of eight subscales, each measuring a specific function within the central nervous system. Each scale ranges from 0 to 6, where 0 is normal and 6 is maximal impairment. The EDSS is an index of MS severity ranging from 0 (normal) to 10 (death). 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, it has been used in most clinical trials [35]. To maximise reproducibility, a single neurologist whose level of intrarater reliability was high (intraclass correlation coefficient, 0.92) performed these assessments. A shift of 1 EDSS point and 2 FSS points was required to determine change.

Disability was assessed by the motor and the cognitive domains of the FIM [13]. The FIM motor section has 13 items which assess the level of functional independence in four subscales, i. e. self-care, transfers, locomotion and sphincter control. The FIM cognitive domain has five items assessing the level of functional independence in two subscales, i. e. language, and cognition. Each item is rated on a scale of 1 to 7 (1 = total assistance required; 7 = independent). This seven-point scale reflects the burden of care required in each area measured. The burden of care is the "substituted time/energy which must be brought to serve the dependent needs of the disabled individuals so that a certain quality of life may be achieved" [13]. The underlying rationale for classifying an activity as "independent" or "dependent" is whether another person (a helper) is required and to what extent. In almost all instances a score of five points reflects need for supervision; a score of four points indicates that physical assistance is required. There is a good evidence to support the reliability and validity of the FIM. All motor and cognitive items of the FIM can be Rasch analysed [37]. 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. We assessed quality of life with the SF-36 [33] and Tempelaar Social Experience Checklist (SET) [30]. Results of outpatient rehabilitation on quality of life have been discussed in another paper [22].

Ethics

The local ethical committee had previously approved the study.

Each patient provided a signed informed consent to participate in this study.

Rehabilitation program

Each patient in the treatment group was treated with a comprehensive rehabilitation program. This considers rehabilitation to be over and above symptomatic treatment and emphasises the achievement of the best possible quality of life, within the limits of the disease. Each patient in the treatment group was treated following an interdisciplinary team assessment (patient, neurologist, physiatrist, physiotherapist, speech therapist, nurse, psychologist, urologist, family member, volunteers), with an individualised, goal-oriented program, addressing a wide range of areas, for six consecutive weeks, six days a week (for more detail see reference 22). The control group was instructed in a home exercise program [23] to be carried out for 12 weeks. The treatment group was also trained in the home exercise program for the further six weeks.

Statistical analysis

There were two outcome measures. The primary was the effect of the rehabilitation program on disability as measured by the different domains of the FIM. The secondary outcome measure was change in neurological impairment as assessed by either the EDSS or its functional systems.

Descriptive statistics were used to describe the characteristics of the sample population in terms of demographics and levels of impairment (FSS and EDSS), and disability (FIM). Repeated ANOVA measures were performed in both treatment and control groups to evaluate the changes of FSS, EDSS, and FIM subscales at weeks 6 and 12. FIM subscales scores in the two study groups were compared by means of the Mann-Whitney U test. In addition, changes were described in terms of percentage of patients who had improved in each of the scales used and were analysed by using Fisher's exact test. The clinical impact of the intervention was assessed by the effect size statistic, calculated as mean change in controls divided by the pooled standard deviation of the baseline mean (Kazis effect) [16]. We used the criteria of Cohen [5] to interpret the effect size, where a value of 0.2 is considered as small effect, 0.5 as moderate, and 0.8 as large.

Results

From a sample of 407 MS patients screened, 111 with EDSS score ranging from 4.0 to 8.0 were enrolled in the study. Of these 111 patients, 58 were assigned to the treatment group and 53 to the control group. Patients characteristics at baseline are summarised in Table 1. The 296 patients who were not randomised included 130 with an EDSS score out of range, 81 on physiotherapy, 55 on immunosuppressive or interferon therapy, 19 in relapse, 8 with concomitant diseases and three who did not wish to participate (Fig.1).

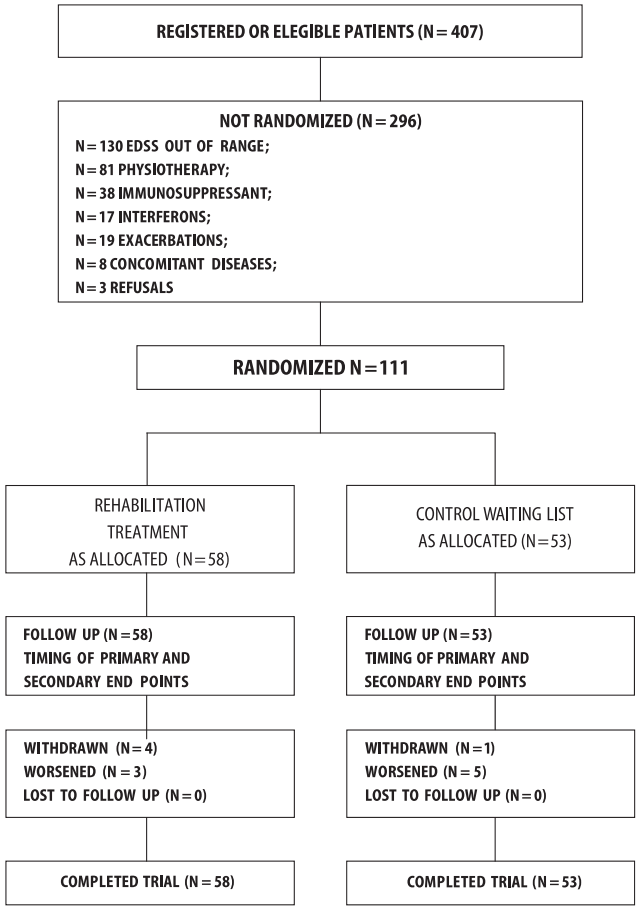

Fig. 1 Flow chart of the randomised controlled trial

Disability

Thirty two patients (55.1 %) of the treatment group and four of the control group improved on the FIM by two or more steps at 12 weeks (Fisher's exact test, $p < 0.0001$). FIM motor domain scores differed significantly in the two groups at 12 weeks, particularly in locomotion, self-care and transfers ($p < 0.001$) (Table 2). The effect size statistic was from moderate to large for locomotion (0.76; 95 % CI −0.4 to + 6.9), self-care (0.73; 95 % CI −0.1 to + 6.8) and transfers (0.65; 95 % CI −0.1 to + 5.9); from small to moderate for sphincter function (0.40; 95 % CI −0.4 to + 3.8). No change was observed in the cognitive subscales of the FIM (effect size 0.03; 95 % CI −0.30 to 0.00). By contrast the control group showed no change.

Impairment

The changes in either EDSS or FSS scores clustered around 0 in both groups at 12 weeks. An improvement by one EDSS step occurred in only two patients assigned to the treatment group and in one patient in the control group. At 12 weeks five patients (8.6 %) in the treatment group and four (7.5 %) in the control group improved by one-half step.

One point improvement was observed in 4 (6.8 %) treatment patients and in 5 (9.4 %) control patients in pyramidal function, in 3 (5.1 %) treatment patients and in 2 (3.7 %) control patients in sensory function, in 3 (5.1 %) treatment patients and in 2 (3.7 %) control patients in cerebellar function, in 2 (3.4 %) treatment patients and in 2 (3.7 %) control patients in brainstem function and only in 1 (1.7 %) treatment patient in sphincter function. No change was observed for any patient in visual and mental functional systems (Table 3).

Table 1 General and clinical findings of patients

	Treatment	Control
Patients	58	53
Age m ± sd (min-max)	45.2 ± 12.0 (25–60)	46.1 ± 6.0 (30–57)
Men	24 (41.4 %)	23 (43.4 %)
Women	34 (58.6 %)	30 (56.6 %)
Disease duration m ± sd (min-max)	17.2 ± 8.1 (5–30)	17.2 ± 4.8 (9–26)
Disease course	n (%)	
primary progressive	12 (20.7 %)	11 (20.8 %)
secondary progressive	46 (79.3 %)	42 (79.2 %)
education, ys mean ± sd	11.3 ± 4.7	11.1 ± 5.1
Mini Mental State Examination	27.4 ± 1.5	27.2 ± 1.8

m mean; *sd* standard deviation

Discussion

These results suggest that impairment, as assessed by the EDSS and functional systems, is not influenced by a short outpatient rehabilitation program. However 55.1 % of the treatment group patients improved their independence level and maintained the benefits gained on the FIM motor domain at 12 weeks. The degree of improvement in disability produced by the rehabilitation

Table 2 Results of rehabilitation on FIM

Variable	Treatment (n = 58)		Control (n = 53)		Effect size Treatment Control (t1)	Baseline-t1	
	Baseline m ± sd	t1 m ± sd	Baseline m ± sd	t1 m ± sd		Treatment	Control
Cognitive	31.9±2.9	32.6±2.3	32.6±3.4	32.5±3.5	0.03	0.8±2.5	–0.1±0.5
Sphincter function	11.6±1.4	12.5±1.3*	11.7±2.8	11.6±2.7	0.40	0.9±1.4	0.0±0.2**
Selfcare	28.6±4.6	32.9±5.7*	28.7±6.8	28.7±6.9	0.73	4.3±4.7	0.0±0.4**
Transfers	12.8±13.5	15.4±3.7*	13.0±4.2	12.9±4.1	0.65	2.6±2.7	–0.1±0.4**
Locomotion	8.0±2.3	9.6±3.1*	7.7±2.7	7.7±2.6	0.76	1.6±2.4	0.0±0.4**
Total FIM	92.9±11.0	103.0±14.3*	93.7±16.4	93.7±16.4	0.68	10.2±11.8	0.0±0.7**

FIM Functional Independence Measure
* $p < 0.001$ vs T_0 ANOVA comparison; ** $p < 0.001$ vs control group Mann Whitney U test

Table 3 Results of rehabilitation on EDSS and the functional system of Kurtzke Scale

Variable	Treatment (n = 58)		Control(n = 53)		Baseline-t1	
	Baseline m ± sd	t1 m ± sd	Baseline m ± sd	t1 m ± sd	Treatment	Control
EDSS	6.2±1.2	6.1±1.2	6.1±1.2	6.2±1.2	NS	NS
Pyramidal	4.2±1.5	4.0±1.4	4.1±1.4	4.2±1.3	NS	NS
Sensory	3.6±1.2	3.3±1.5	3.7±1.2	3.7±1.1	NS	NS
Cerebellar	3.5±1.2	3.4±1.2	3.6±0.9	3.5±0.9	NS	NS
Brainstem	2.7±1.9	2.5±1.8	2.8±1.3	2.9±1.1	NS	NS
Sphincter	3.1±1.2	3.0±1.0	3.0±1.3	3.2±1.2	NS	NS
Visual	2.9±1.3	2.9±1.3	3.1±1.2	3.1±1.2	NS	NS
Mental	0.9±0.7	0.8±0.7	0.9±0.6	0.9±0.6	NS	NS
Other	0.4±0.6	0.4±0.5	0.5±0.6	0.5±0.5	NS	NS

EDSS Expanded Disability Status scale; *m* mean; *sd* standard deviation

treatment was clinically useful, as indicated by increased scores in all FIM motor domain scales, with large (locomotion) or moderate (self care and transfers) effect sizes. This improvement was modest in sphincter function.

Our data are in accordance with the published waiting-list randomised study of Freeman et al. on progressive MS patients [12]. In fact in this study a large percentage of people in the treatment group improved their overall level of disability; this effect was evident in all motor domains of the FIM scale: self-care, transfers, sphincter function. For locomotion the effect was limited to the wheelchair restricted patients. This study is different from ours because it was based on an inpatient population with higher percentage (47%) of very severely disabled patients (EDSS 7.0–9.5) and a control intervention was lacking. A significant reduction of handicap as assessed by the London Handicap Scale was also found [15]. In our study there was a minor percentage of very severely disabled with only 8% patients at EDSS 8.0. As in the Freeman study et al. [11], benefits gained from rehabilitation were maintained for a period lasting from 4 to 6 months (data not shown). Similar evidence was also provided by Solari et al., who demonstrated that the benefits of a three-week rehabilitation program persisted for nine weeks in mobility, self-care and locomotion and for 15 weeks in self-care and locomotion. The study population consisted of both inpatients and outpatients; a small percentage of patients in the relapsing remitting phase of the disease was included and patients were treated with specific exercises, consisting of passive (stretching, mobilisation) and active interventions [28]. In contrast, we only admitted outpatients in the progressive phase of the disease with a mean higher level of impairment, treated with a comprehensive multidisciplinary goal-oriented rehabilitation program, including occupational, psychological and speech therapy. Despite these differences, these three studies showed a positive effect of rehabilitation treatment on disability (as assessed by the FIM) and a negligible effect on impairment. Furthermore the results obtained were persisting for several months.

Another randomised study of Petajan et al. clearly demonstrated that exercise training improved fitness and had a positive impact on factors related to quality of life (QoL) [24]: a 15-week aerobic training (40 minutes

each session, 3 times a week) improved maximal aerobic capacity, upper and lower extremity strength and significantly reduced skinfolds, triglycerides, and very-low-density lipoprotein. Depression, anger and fatigue also improved in the exercise group. EDSS scores were unchanged, except for improved bowel and bladder function in the exercise group.

Few of the studies underlining the positive effect of outpatient rehabilitation programs in MS focused on the progressive form of the disease [8, 10, 22]. Evidence was provided by Francabandera et al. who demonstrated that the inpatient treated group showed less disability than the outpatient group in advanced SPMS. However, the initial advantage of inpatient over outpatient treatment was short-lived [10]. In contrast, although our patients were less disabled than those enrolled by Francabandera et al., our results showed that outpatient rehabilitation minimised disability and improved QoL [22].

Finally it has been pointed out that physical health and QoL in MS are influenced by family and social support [18, 21]. The management of these aspects of care may not be feasible in the context of an inpatient model. Considering this Shapiro et al. [27] developed a "maintenance" rehabilitation program which could be regarded as "extended" home outpatient rehabilitation. This extended exposure to rehabilitation (5 hours, 1 day a week for one year) produced substantial benefit in patients with chronic progressive MS. Patients who participated in this treatment program experienced fewer symptoms, less fatigue, and had a lower rate of decline in physical function compared with subjects of the waiting-list [8].

A more recent study by Wiles et al. showed that a course of physiotherapy improved the mobility of MS patients who walk 5 meters with or without a mechanical aid. The authors concluded that physiotherapy improves subjective well being and mood and that there was no difference in efficacy between home and hospital based therapy. They also found that home therapy was more costly [34]. In contrast to our study, these authors found that benefits gained by rehabilitation may only last a few weeks. This difference can be partly explained by the fact that these authors included only patients able to walk with or without aid, used different measurement instruments to evaluate disability and gave a shorter course of physiotherapy.

Based on the results of our study, which supports the previously demonstrated effectiveness of rehabilitation for people with MS, it can be stated that rehabilitation is an effective therapeutic intervention in MS. This study does not define the optimum rehabilitation strategy but it is evident that a multidisciplinary rehabilitation package offered as outpatient treatment is more effective on disability than home therapy. This rehabilitation strategy was well accepted; in fact no patient was lost to follow-up.

Our randomised controlled study performed with an outpatient rehabilitation program demonstrated that a 6 week course of a comprehensive rehabilitation program (six days a week) resulted in significant improvement of self-care, transfers and locomotion, with a slight improvement of sphincter function. These benefits were clinically significant and relatively low in cost.

Further studies are warranted in order to evaluate the effectiveness of inpatient rehabilitation program versus outpatient rehabilitation program or home therapy and the cost benefit ratio of each model of rehabilitation treatment should be further analysed.

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