Efficacy of a Physical Therapy Program in Patients With Parkinson's Disease: A Randomized Controlled Trial

Terry Ellis, MSPT, Cees J. de Goede, MSPT, Robert G. Feldman, MD, Erik C. Wolters, MD, Gert Kwakkel, PhD, Robert C. Wagenaar, PhD

ABSTRACT. Ellis T, de Goede CJ, Feldman RG, Wolters EC, Kwakkel G, Wagenaar RC. Efficacy of a physical therapy program in patients with Parkinson's disease: a randomized controlled trial. Arch Phys Med Rehabil 2005;86:626-32.

Objective: To investigate the effects of a physical therapy (PT) program in groups of people with Parkinson's disease (PD).

Design: Randomized controlled trial with a crossover design.

Setting: Two outpatient rehabilitation clinics in Boston and Amsterdam, respectively.

Participants: Sixty-eight subjects diagnosed with typical, idiopathic PD, Hoehn and Yahr stage II or III, and stable medication use.

Intervention: Group A received PT and medication therapy (MT) for the first 6 weeks, followed by MT only for the second 6 weeks. Group B received only MT for the first 6 weeks and PT and MT for the second 6 weeks.

Main Outcome Measures: The Sickness Impact Profile (SIP-68), the mobility portion of the SIP-68, the Unified Parkinson's Disease Rating Scale (UPDRS), and comfortable walking speed (CWS) at baseline, 6-week, 12-week, and 3-month follow-up.

Results: At 6 weeks, differences between groups were significant for the SIP mobility (P=.015; effect size [ES]=.55), for CWS (P=.012; ES=.49), for the activities of daily living (ADL) section of the UPDRS (P=.014; ES=.45), and for the total UPDRS (P=.007; ES=.56). The total SIP and the mentation and motor sections of the UPDRS did not differ significantly between groups. Significant differences were found at 3 months compared with baseline for CWS, the UPDRS ADL, and total scores.

Conclusions: People with PD derive benefits in the short term from PT group treatment, in addition to their MT, for quality of life related to mobility, CWS, and ADLs; long-term benefits were found in CWS, UPDRS ADL, and total scores but varied between groups.

Key Words: Parkinson disease; Physical therapy; Randomized controlled trials; Rehabilitation.

PARKINSON'S DISEASE (PD) is a progressive neurologic disorder characterized by insidious onset. The first clinical signs occur when about 60% of the dopamine-producing cells in the substantia nigra have degenerated.[1] The mean age of onset of PD is in the mid fifties, with increasing incidence and prevalence as age increases.[2] With an estimated prevalence of 128 to 187 per 100,000 and an annual incidence of 20 per 100,000, PD is among the most common neurologic diseases.[3] Despite dopaminergic medication, dopamine agonists, monoamine oxidase type B inhibitors, catechol *O*-methyltransferase inhibitors, and in some cases surgical intervention, people face a relentless deterioration in mobility and activities of daily living (ADLs). The clinical hallmarks of the disease include rigidity, bradykinesia, tremor, and loss of postural control.[4] These impairments lead to a decline in functional status such that people with PD have difficulty with tasks such as walking, rising from a chair, and moving in bed. This decrease in functional status often results in a loss of independence and a decline in quality of life (QOL). The rate of progression varies widely among the PD population, ranging from 2 to 30 years until severe disability or death.[2] Given the large number of people affected by this disease, the long life span after diagnosis, the progressive nature of PD, and the short duration of medication effectiveness, it is critical to identify additional interventions to maximize QOL and functional status while minimizing the burden on society.

A number of intervention studies have investigated the efficacy of physical therapy (PT) and medication therapy (MT) in people with PD. Most studies reveal the positive effects of PT in patients with PD. A meta-analysis[5] of 12 studies, classified as true or quasi-experiments, investigating the effects of PT and medications in subjects with PD showed a significant summary effect size (ES) for ADLs (.40), stride length (.46), and walking speed (.49). The summary ES for neurologic signs (.22) was not significant. A meta-analysis[6] of 16 studies investigating the effects of occupational therapy (OT)−related treatments for subjects with PD revealed a significant summary ES for outcomes classified at the capabilities and abilities level (.50), the activities and tasks level (.54), and on overall outcomes (.54). The results of this meta-analysis also suggested small to moderate positive effects of OT-related interventions in subjects with PD. In both systematic reviews by Deane et al,[7,8] however, it was concluded that there was not enough evidence to reject or to support the efficacy of PT for patients with PD. Marked methodologic flaws of most of the studies in the authors' opinions, did not allow for a meta-analytic review of the data presented. In addition to the methodologic flaws in the PD rehabilitation literature, there is also a lack of emphasis on measuring QOL changes after participation in a rehabilitation program. Focus has been on impairment-level changes in motor status and on changes in function with regard to mobil-

From Sargent College of Health and Rehabilitation Sciences, Department of Rehabilitation Sciences and Center for Neurorehabilitation, Boston University, Boston, MA (Ellis, Wagenaar); Boston Medical Center, Boston, MA (Feldman); Departments of Physical Therapy (de Goede, Kwakkel) and Neurology (Wolters), Vrije Universiteit Medical Center, Amsterdam, Netherlands; and Research Institute for Fundamental and Clinical Human Movement Sciences, Amsterdam, Netherlands (Kwakkel).

Presented as a poster to the American Physical Therapy Association, February 12–16, 2003, Tampa, FL.

No commercial party having a direct financial interest in the results of the research supporting this article has or will confer a benefit upon the author(s) or upon any organization with which the author(s) is/are associated.

Correspondence to Terry Ellis, MSPT, Boston University, Sargent College of Health and Rehabilitation Sciences, 635 Commonwealth Ave, Boston, MA 02215, e-mail: *tellis@bu.edu.* Reprints are not available from the authors.

0003-9993/05/8604-9097$30.00/0

doi:10.1016/j.apmr.2004.08.008

ity, but the impact of rehabilitation on QOL is largely unknown.

The primary objective of our study was to investigate the efficacy of group PT intervention in subjects with PD across 2 sites by conducting a large randomized controlled trial (RCT) with QOL as the primary outcome measure. In this RCT, it was hypothesized that people in the early to middle stages of PD participating in a group PT program 1.5 hours, 2 days a week for 6 weeks, added to MT, would benefit in terms of QOL, functional status, and neurologic impairments compared with a control condition of MT only. In addition, it was hypothesized that subjects would show a larger gain during the intervention period than during the control period and that these gains would be maintained for 3 months postintervention.

METHODS

Participants

A total of 68 subjects diagnosed with typical, idiopathic PD participated in this study, which was conducted at 2 sites. Thirty-seven subjects participated at the Boston site in the United States, and 31 participated at the Amsterdam site in the Netherlands. At the Boston site, subjects were recruited from the Department of Neurology at Boston Medical Center and from local support groups in the Boston area. At the Amsterdam site, subjects were recruited from the Department of Neurology at Vrije Universiteit Medical Center. All subjects met the following inclusion criteria: (1) stable medication usage; (2) Hoehn and Yahr stage II or III; (3) at least 1 score of 2 or more for at least 1 limb for either the tremor, rigidity, or bradykinesia item of the Unified Parkinson's Disease Rating Scale (UPDRS); (4) ability to walk independently; (5) age 35 to 75 years; (6) no severe cognitive impairments (Mini-Mental State Examination score, $\geq$24); (7) no other severe neurologic, cardiopulmonary, or orthopedic disorders; and (8) not having participated in a PT or rehabilitation program in the previous 2 months. All subjects were required to sign an informed consent document approved by the institutional review boards at Boston University and Vrije Universiteit Medical Center.

Study Design

This study was an RCT with a crossover design, taking place during a 6-month period (fig 1). Recruitment began in 1997, and the study was completed in 2001. A power analysis based on the Sickness Impact Profile (SIP-68), our primary outcome measure, indicated that a minimum of 60 subjects was necessary to have sufficient power (based on an estimated ES of 0.4) to detect differences in efficacy between the 2 conditions.[5] Within each site, 8 subjects were randomly allocated to 2 groups by the investigators who were not involved in data collection, treatment implementation, or data analysis. A block randomization procedure was used in which each sealed envelope contained 4 group A assignments and 4 group B assignments. This process continued until a total of 68 subjects were randomly allocated. Subjects in group A started with a 6-week PT program added to their MT, followed by a 6-week control period during which only MT was received. Subjects in group B began with an initial 6-week control period consisting of MT only, followed by a 6-week intervention period consisting of both PT and MT. The PT program comprised 12 sessions, each 1.5 hours long, 2 times a week during a 6-week period. Baseline assessments were done before randomization (t0), after the initial 6 weeks (t6), and after the second 6-week period (t12). A final assessment was conducted 3 months (t24) after the second 6-week period. An investigator blinded to group assignment conducted all assessments. For each subject, all assessment sessions were performed at the same time of day, and all tests were performed in the same order, to control for variations in performance because of medication cycle. All assessments were conducted in the "on" state for those subjects experiencing motor fluctuations. All subjects were required to take their medications at the same time of day for all assessment sessions.

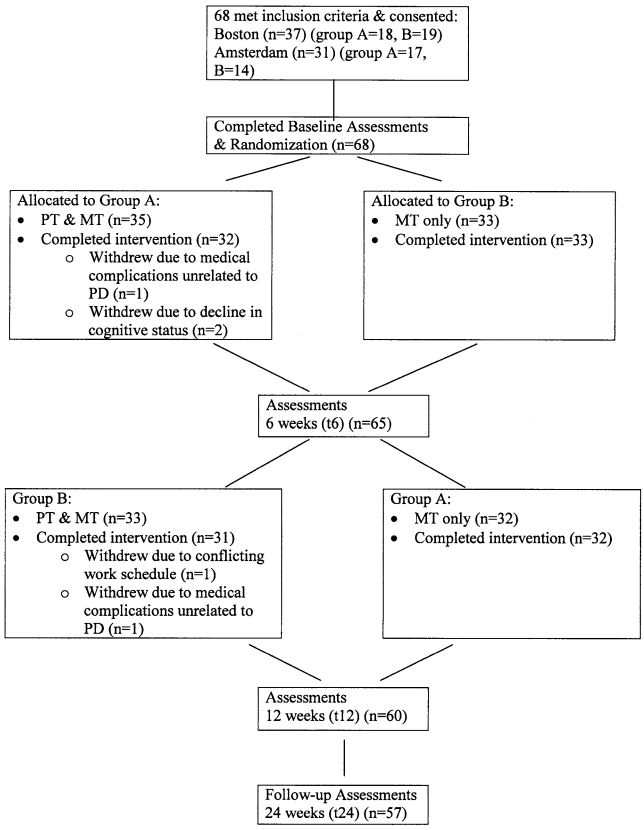

Fig 1. Study design and flow of participants through each stage of the trial.

Assessments

The SIP-68[9] is a modified version of the SIP-136. It explains 94% of the total variance of the original SIP-136. Although the SIP was originally designed to assess changes in behavior as the result of disease, recent intervention studies have shown it to be responsive to detect treatment efficacy.[10] Six domains of health-related functional status (ie, somatic autonomy, mobility control, psychological autonomy and communication, social behavior, emotional stability, mobility range) were evaluated by using the SIP-68.[11] Scores from 3 of these domains (ie, somatic autonomy, mobility control, mobility range) were used to comprise the SIP mobility score. These mobility domains consist of items evaluating functional mobility, ADLs, and instrumental ADLs such as housecleaning, shopping, or washing clothes. A high score indicates poor health-related functional status. Post et al[11] have shown that the instrument is valid and highly reliable. Sections I, II, and III of the UPDRS were used to assess impairments and functional status.[12] Section I consists of 4 items measuring mentation, behavior, and mood. Section II measures ADLs and consists of 13 items (eg, dressing, falling, walking, turning in bed, cutting food). The information in sections I and II was obtained through subject

interview. Section III measures the motor system status and consists of 14 items (eg, severity of rigidity, bradykinesia, and tremor, as well as coordination of rapid alternating movement of the upper and lower extremities). The information was obtained through examination. Each item in all sections is rated on a 5-point ordinal scale. The UPDRS has been administered in several large clinical trials and is reliable and valid.[12] Comella et al[13] have shown the responsiveness of the total UPDRS score and the ADL and motor subsections.

To assess comfortable walking speed (CWS), subjects were asked to walk on the treadmill without holding on for support. For safety, standby supervision was provided, but no physical assistance was given. Subjects were allowed a 5-minute practice period to become accustomed to the treadmill. The researcher proceeded to gradually increase the speed of the treadmill, asking the subject to identify when walking pace was most comfortable. Subjects were not aware of the numerical value associated with walking speed, in an effort to avoid encouraging them to replicate a previously attained walking speed or to walk faster. The speed was repeatedly decreased and increased around the CWS, to facilitate subjects' ability to distinguish slow, comfortable, and fast walking speeds. Measuring walking velocity on a treadmill is both a valid and a reliable measure.[14] Gait velocity is a clinically relevant outcome measure and is responsive in several patient populations, including those diagnosed with PD.[15,16]

Rehabilitation Program

The rehabilitation program consisted of 12 sessions, each 1.5 hours long, 2 times a week for 6 weeks. All treatment sessions occurred at the same time of day on the same 2 days of the week throughout the study. Intervention was conducted in a group format, in which 4 subjects participated in the program led by 1 licensed physical therapist and assisted by 1 to 2 PT students. A total of 3 licensed physical therapists at each site participated in 2 training sessions in the treatment outlined by the investigators. The physical therapists involved in performing the intervention were not involved in conducting any assessments. The treatment consisted of cardiovascular warm-up activities (5min), stretching exercises (15min), strengthening exercises in a functional context (15min), functional training (15min), gait training overground and on a treadmill with external auditory cueing (15min), balance training and recreational games (15min), and relaxation exercises (10min). There is evidence in the literature to support each of the components contained in the intervention.[16-22]

Statistical Analysis

The following findings would support the hypothesis that the PT program was beneficial in terms of QOL, functional limitations, and neurologic impairments: (1) during the first 6 weeks (t0 to t6), group A should show a greater improvement than group B; (2) group A should show a greater improvement during the rehabilitation period (t0 to t6) than during the control period (t6 to t12); (3) group B should show a greater improvement during the rehabilitation period (t6 to t12) than during the control period (t0 to t6); (4) if group A improves during the intervention period, the gains will be maintained after the control period (t6 to t12) in comparison with baseline measurements; and (5) if both groups improve during the intervention periods, these gains will be maintained (t24) in comparison with baseline measurements (t0 to t24).

Differences in baseline outcome measures between groups were analyzed by using the Mann-Whitney *U* test. Two-way analysis of variance (ANOVA) with repeated measures was used to analyze for main effects of group and time and the interaction effect between group and time. If a significant interaction effect for time and group was found, the following post hoc analyses were performed: (1) a between-group (group A vs group B) comparison with respect to the first 6 weeks (t0 to t6) of the design using a contrast analysis (hypothesis 1), (2) a within-group comparison between rehabilitation and control periods (change scores from t6 to t0 vs t12 to t6) by using a Wilcoxon signed-rank test (hypotheses 2, 3), and (3) a comparison between follow-up and baseline measures (t24 vs t0) for both groups by using a Wilcoxon signed-rank test (hypotheses 4, 5). The level of significance was set at .05. For each outcome, the ES of Hedge's *g* and the 95% confidence interval (CI) were calculated. The ES of *g* was calculated by taking the difference between the means of group A and group B divided by the average population standard deviation (SD). To estimate the SD for *g*, baseline estimate SDs of groups A and B were pooled.[23] All data analyses were performed by using the SPSS Professional Statistics, version 10.1 software,[a] for Windows.

RESULTS

A total of 68 subjects (37 from Boston, 31 from Amsterdam) met the inclusion criteria, consented to participate, completed baseline assessments, and were randomly allocated to either group A or group B (see fig 1). All subjects completed all baseline assessments except for the UPDRS, which was not administered to 11 subjects admitted to the study. Sixty-three subjects completed the intervention. Two subjects withdrew from treatment because of medical complications unrelated to PD, 2 withdrew because of a decline in cognitive status, and 1 withdrew secondary to a conflicting work schedule. Sixty-five subjects participated in assessments at t6. The 3 subjects who withdrew during the intervention period did not participate in assessments at t6. Sixty subjects participated in assessments at t12. Two subjects who did not complete the intervention did not participate in assessments at t12. In addition, 3 other subjects had scheduling conflicts and were not included in assessments at t12. Fifty-seven subjects participated in assessments at t24. Three additional subjects were lost to follow-up, 1 because of unrelated medical complications and 2 because of scheduling conflicts.

Data from 68 subjects were used to perform the analysis on baseline characteristics, SIP, SIP motor, and CWS. Data from 57 subjects were used to perform the baseline analysis on all sections of the UPDRS. Analyses at t6, t12, and t24 were performed on those subjects with complete data sets (tables 1, 2). Subjects with missing data were excluded from the initial analysis.

A subject's attendance in the rehabilitation program was recorded at each session to monitor compliance. Of the 68 subjects, 50 attended all treatment sessions, 10 missed 1 session, 4 missed 2 sessions, and 1 missed 3 sessions. Three subjects dropped out after t0 and did not attend any treatment sessions.

In table 3, the baseline characteristics (ie, age, sex, Hoehn and Yahr stage) and baseline intake values of all dependent variables are presented for all subjects combined, for groups A and B separately, and for site 1 and 2 separately. Baseline characteristics and intake values for all dependent measures of subjects in group A did not differ significantly from those in group B. Baseline characteristics of subjects at site 1 did not differ significantly from those at site 2. However, there were significant differences between sites with respect to baseline SIP total, SIP motor, UPDRS III, UPDRS total, and CWS scores, which suggests differences in disease severity between

Table 1: Baseline Values and Changes From Baseline for All Outcome Measures

Variable	Group	Measurements			
		Baseline	6 Weeks	12 Weeks	24 Weeks
SIP	A	85.0±9.5	−1.5±5.3	−1.3±3.9	−0.2±4.7
	B	83.4±8.2	−0.5±4.4	0.5±5.3	1.3±5.9
SIP mobility	A	46.1±4.9	−1.5±3.1*	−0.8±2.9†	−0.7±2.9
	B	45.0±4.0	0.2±2.7*	0.3±2.5	0.9±2.8
UPDRS I (mentation)	A	3.1±1.8	−1.1±1.6	−0.8±1.3	−1.0±1.6
	B	3.0±1.8	−0.5±1.3	−0.9±1.3	−0.4±2.0
UPDRS II (ADLs)	A	13.2±4.6	−2.1±2.8*	−2.2±2.8†	−1.8±3.2‡
	B	13.0±4.1	−0.3±2.3*	−1.0±3.1	−0.0±3.2
UPDRS III motor	A	28.9±8.4	−3.0±6.6	−2.6±7.8	−3.5±8.6
	B	31.5±7.8	−0.2±5.3	−1.4±5.2	−1.5±6.7
UPDRS total	A	45.3±10.7	−6.2±6.2*	−5.7±8.5†	−5.3±11.6‡
	B	47.4±10.7	−1.0±6.0*	−3.4±7.4	−1.9±8.1
CWS	A	.77±.30	.16±.22*	.14±.25†	.06±.24
	B	.83±.34	.01±.21*	.19±.29†	.09±.24‡

NOTE. Values are mean ± SD. A decrease in SIP, SIP mobility, and all UPDRS scores indicates an improvement in status. Within-group analyses were performed only on those measures for which a significant interaction effect between group and time was found. Statistical significance set at $P<.05$.
*Significant between-group differences (contrast analysis).
†Significant differences within groups comparing intervention and control periods (Wilcoxon signed-rank test).
‡Significant differences between follow-up and baseline periods (Wilcoxon signed-rank test).

the 2 samples. No significant differences in baseline UPDRS I and II scores with respect to sites were found.

For the SIP-68, no significant interaction effect between group and time was observed. In addition, no significant main effects for group or time were revealed (see tables 1, 2). An ES for the total SIP score of 0.1 (95% CI, −.44 to .64) is consistent with our lack of significant findings on this global QOL measure.

A significant interaction effect between group and time was found for the SIP mobility scores. Post hoc analysis revealed a significant difference between groups ($P=.015$) after the initial 6-week intervention period (t0 to t6), which indicates a significantly improved QOL score as it relates to physical mobility compared with the control period (see table 2). An ES for the SIP mobility score of .55 (95% CI, 0.0−1.1) is consistent with these significant findings. No significant main effects for group and time

Table 2: Group Comparisons

Variable	ANOVA (t0 to t12)			Post Hoc Analysis (t0 to t6)	
	G	T	T×G	T	T×G
SIP total	*df*=1,57	*df*=2,114	*df*=2,114		
Group A (n=30)	F=.02	F=1.66	F=.91		
Group B (n=29)	(NS, *P*=.88)	(NS, *P*=.20)	(NS, *P*=.41)		
SIP motor	*df*=1,57	*df*=2,114	*df*=2,114	*df*=1,57	*df*=1,57
Group A (n=30)	F=.03	F=1.76	F=3.48	F=3.24	F=6.3
Group B (n=29)	(NS, *P*=.88)	(NS, *P*=.18)	(*P*=.034)	(NS, *P*=.08)	(*P*=.015)
UPDRS I	*df*=1,48	*df*=2,96	*df*=2,96		
Group A (n=25)	F=.17	F=12.2	F=.81		
Group B (n=25)	(NS, *P*=.68)	(*P*<.001)	(NS, *P*=.48)		
UPDRS II	*df*=1,48	*df*=2,96	*df*=2,96	*df*=1,48	*df*=1,48
Group A (n=25)	F=.90	F=9.8	F=2.96	F=11.1	F=6.58
Group B (n=25)	(NS, *P*=.35)	(*P*<.001)	(*P*=.057)	(*P*=.002)	(*P*=.014)
UPDRS III	*df*=1,48	*df*=2,96	*df*=2,96	*df*=1,48	*df*=1,48
Group A (n=25)	F=5.35	F=3.05	F=.99	F=3.09	F=2.2
Group B (n=25)	(*P*=.025)	(NS, *P*=.52)	(NS, *P*=.38)	(NS, *P*=.085)	(NS, *P*=.145)
UPDRS total	*df*=1,48	*df*=2,96	*df*=2,96	*df*=1,48	*df*=1,48
Group A (n=25)	F=4.88	F=11.4	F=2.7	F=17.0	F=8.05
Group B (n=25)	(*P*=.032)	(*P*<.001)	(*P*=.069)	(*P*<.001)	(*P*=.007)
CWS (m/s)	*df*=1,59	*df*=2,118	*df*=2,118	*df*=1,59	*df*=1,59
Group A (n=31)	F=.01	F=15.5	F=5.5	F=11.3	F=6.67
Group B (n=30)	(NS, *P*=.94)	(*P*<.001)	(*P*=.005)	(*P*=.001)	(*P*=.012)

NOTE. Results of statistical analysis for all patients between groups A and B, with respect to total SIP score; SIP motor score; UPDRS sections I, II, III, and total; and CWS during the first 12 weeks (t0 to t12) and during the first 6 weeks (t0 to t6).
Abbreviations: G, group; NS, not significant; T, time.

Table 3: Baseline Characteristics of All Study Participants Expressed in Total, by Group and Site

Variable	All Subjects	Group A	Group B	Boston	Amsterdam
Patients (n)	68	35	33	37	31
Age (y)	64±8.6	64±8.4	63±8.8	64±8.8	63±8.5
Hoehn and Yahr	2.4±0.5	2.5±0.5	2.4±0.5	2.4±0.4	2.5±0.6
Sex (M/F)	51/17	25/10	26/7	30/7	21/10
SIP total score	84.3±8.9	85.0±9.5	83.4±8.2	86.2±8.9*	81.9±8.3*
SIP motor score	45.6±4.5	46.1±4.9	45.0±4.0	47.0±4.5*	43.8±4.0*
UPDRS I score	3.1±1.8	3.1±1.8	3.0±1.8	3.0±1.9	3.2±1.6
UPDRS II score	13.1±4.3	13.2±4.6	13.0±4.1	13.2±4.0	13.0±5.0
UPDRS III score	30.2±8.1	28.9±8.4	31.5±7.8	32.0±7.3*	26.8±8.6*
UPDRS total score	46.3±10.7	45.3±10.7	47.4±10.7	48.2±9.8*	42.9±11.7*
CWS (m/s)	0.8±0.3	.08±0.3	0.8±0.3	0.9±0.3*	0.7±0.3*

NOTE. Values are mean ± SD. There were no significant differences in baseline characteristics between groups.
Abbreviations: F, female; M, male.
*Significant difference between sites ($P<.05$).

were found. A within-group analysis for group A showed significantly larger improvements ($P=.019$) in SIP mobility change scores during t0 to t6 compared with t6 to t12 (see table 1). However, these gains were not sustained after the control period because there was no significant difference from t0 to t12 in group A. A within-group analysis for group B revealed no significant differences between the control period and the intervention periods (see table 1). With regard to long-term effects, a comparison between baseline (t0) and follow-up (t24) SIP mobility scores showed no significant differences for either group A or group B (see table 1). The latter finding indicates that at 24 weeks post-study, subjects' QOL, as measured by the SIP mobility, was similar to baseline status.

An interaction effect between group and time approached significance ($P=.069$) for the total UPDRS scores. In addition, a significant main effect for group was found warranting further post hoc analysis. Post hoc analysis revealed a significant difference between groups at t6 ($P=.007$), which indicates a significantly improved status in group A after the intervention period compared with group B during the control period (see table 2). An ES of .56 (95% CI, .28 to .84) for the total UPDRS score supports these findings. A significant main effect of time was found ($P=.001$), which indicates that both groups improved over time. A within-group analysis for group A revealed a significant improvement ($P=.04$) between total UPDRS change scores from t0 to t6 to t6 to t12. These gains were maintained during the control period because there was a significant difference ($P=.002$) between t0 and t12 in group A. A comparison between t0 and t24 revealed a significant difference for group A ($P=.021$), which indicates that the long-term effects were maintained. A within-group analysis for group B, comparing the control period with the intervention period, was not statistically significant. No significant long-term effects were found for group B (see table 1).

No significant interaction effect between group and time was observed for the UPDRS I (mentation, behavior, mood) scores (see table 2). However, there was a significant main effect for time. No significant main effect for group was found. An ES of .38 (95% CI, −.17 to .93) for the UPDRS section I (mentation) supports these nonsignificant findings.

For the UPDRS II (ADL) scores, the interaction effect between group and time approached significance ($P=.057$), warranting further post hoc analysis. Post hoc analysis revealed a significant difference between groups ($P=.014$) after the initial 6-week intervention period (t0 to t6), which indicates an improved ADL score in group A compared with the control period in group B (see table 2). An ES of .45 (95% CI, −.01 to 1.0) for the UPDRS ADL section revealed a small to moderate ES consistent with these findings. No significant main effect for group was found. However, a significant main effect of time was found ($P<.001$). A within-group analysis for group A approached significance ($P=.099$) in ADL change scores from t0 to t6 to t6 to t12. These gains were maintained during the control period because there was a significant difference ($P<.001$) between t0 and t12 in group A. A comparison between t0 and t24 revealed significant long-term effects for group A ($P=.010$). A within-group analysis for group B, comparing the control with the intervention period, was not significant (see table 1).

No significant interaction effect between group and time was observed for the UPDRS III (motor) scores. However, there were significant main effects for both group and time, warranting further post hoc analysis. Post hoc analysis at t6 revealed that differences between groups were not significant ($P=.145$) (see table 2). An ES of .32 (95% CI, −.23 to .86) for the UPDRS section III (motor) supports our lack of significant findings on the impairment level. A within-group analysis revealed no significant difference between scores in period t0 to t6, compared with t6 to t12 for either group (see table 1).

A significant interaction effect between group and time was observed for CWS. Post hoc analysis revealed a significant difference between groups ($P=.012$) after the initial 6-week intervention period (t0 to t6), which indicates significantly improved CWS in group A compared with the control period in group B (see table 2). An ES of .49 (95% CI, 0.00−1.05) for CWS supports these findings. No significant main effect for group was found. However, a significant main effect for time was observed. A within-group analysis for group A revealed significantly higher ($P=.007$) CWS change scores for t0 to t6 compared with t6 to t12. These gains were sustained after the control period because there was a significant difference ($P=.002$) from t0 to t12 in group A. A within-group analysis for group B also revealed significantly larger improvements during the intervention period (t6 to t12) than during the control period (t0 to t6, $P=.041$). With regard to long-term effects, a comparison of t0 and t24 scores showed no significant differences for group A, but significant differences for group B ($P=.005$) were found (see table 1).

DISCUSSION

The findings of our present study partially support our main hypothesis in that gains were observed in functional status and quality of life related to physical mobility but not in global

quality of life or at the impairment level. Our results reveal significant improvements in the SIP motor score, UPDRS ADL score, UPDRS total score, and CWS in the intervention group (PT and medication), compared with the control group (medication only). No significant differences between groups were found for the SIP and UPDRS mentation and motor scores. The within-group analyses supported the between-group differences. Significant differences at 3 months compared with baseline were found for the UPDRS total and ADL scores in group A and for CWS in group B, which indicates that some gains were maintained over time.

An additional analysis using age and sex as covariates did not alter the results or significance levels appreciably for any of the dependent measures. An analysis (worst-case analysis) was also conducted based on the assumption that subjects with missing data at t6, t12, and t24 showed no changes compared with baseline measurements. This did not change the outcome with regard to significance level for any of the dependent variables. Analyses performed by site were consistent with the overall results as well.

We considered the clinical relevance of our significant findings. A classification of walking disability, developed by Hoffer et al[24] and revised by Perry et al,[25] discriminates between a physiologic walker, a limited household walker, a household walker, a limited community walker, and a community walker. In a study of 147 patients poststroke, Perry found that walking velocity was the only single measure that predicted walking classification. In our study, the mean gain in walking velocity was .16m/s. In group A, a gain of 21% from a walking velocity of .77 to .93m/s translates to a change from a limited community walker to a community walker. Similar gains were seen in group B. This suggests that the changes in CWS that occurred appear to be clinically relevant. Significant correlation coefficients were found between the UPDRS ADL section and the SIP mobility in both group A and group B after treatment, suggesting a relationship between change in ADL status and QOL as it relates to physical mobility. The degree of change necessary to be clinically relevant needs further investigation in these measures.

The crossover design may have been a limitation in some respects. We found within-group differences between the intervention and control periods in group A with regard to most of the outcome measures. However, in group B, we observed significant within-group differences with regard to CWS only. Group B often made gains in status during the initial control period and continued to improve during the intervention period. Differences between these periods may have been minimized by the initial gains observed during the control period, which reveals a possible placebo effect. Limitations to our study also include lack of a full data set from the UPDRS. The UPDRS was not administered to 11 subjects admitted to our study. This may have hampered the statistical power of the design and contributed to our results approaching level of significance in the UPDRS motor section. Differences in the impact of rehabilitation on neurologic impairments have been reported. It may be that PT does not affect changes in rigidity or tremor.[5] Even when significant changes in bradykinesia or rigidity are identified, they are short-lived and no longer exist at follow-up.[13] Differences may also be explained by variations in the components of the particular treatments, with some focusing more on the impairment level than others. It is also possible that the UPDRS motor section does not contain measures of the types of impairments where we expect to see change. Some studies[17,18,26,27] report changes in strength and muscle length but not in rigidity and tremor. The relationship between impairments and functional status is also open to further investigation. However, in an RCT, Schenkman et al[17] showed improved axial mobility and functional reach in subjects with PD who participated in a 10-week exercise program focusing on improving spinal flexibility. It was concluded that increases in ability to reach forward in the functional reach test might have been because of the improved spinal mobility. It is also possible that neurologic signs change at the functional level but not at the impairment level. For example, tremor often appears to be altered while walking; however, frequently used measurement tools evaluate tremor independent of function, failing to capture the changes that occur with walking.[15]

Another limitation of our study may be the differences observed in baseline dependent measures between the 2 sites. The differences highlight varying degrees of disease severity at each of the 2 sites, although all were categorized in Hoehn and Yahr stages II and III. The block randomization procedure implemented at each site, however, did result in similar baseline status between the experimental and control groups at each site and across sites. In addition, similar trends were revealed at each of the 2 sites. Several other studies obtained similar results in other samples of subjects in Hoehn and Yahr stage II and III. Generalizability of our results, however, may be limited to community-dwelling people with PD in Hoehn and Yahr stage II and III. In addition, changes in CWS observed on the treadmill may not generalize to changes in CWS over ground. However, several other studies[16,28] report significant changes in overground walking velocity, lending support to our findings.

Our findings revealed changes in QOL at the disability level as it relates to physical mobility (SIP mobility) and at the functional level (walking speed, ADLs), but not at the impairment level (mentation, motor status) or at the global disability level (SIP total). At the disability level, QOL measures are consistently missing from well-controlled PD intervention studies. Our results revealed a significant change in the SIP mobility score but not in the SIP total score. This implies that changes in QOL are limited to those areas affecting physical mobility. There appears to be a specificity of training effect. Treatment aimed at improving function resulted in perceived improvements in QOL related to mobility. Lack of improvements in the more global QOL measure may be secondary to lack of treatment specifically addressing areas beyond physical mobility. To see greater participation in household and community activities, treatment may need to explicitly include practice of these types of activities. Treatment administered in the home environment may be necessary to allow direct instruction in the environment in which the behavioral change is desired. Nieuwboer et al[29] found positive effects for a home PT program for subjects with PD in the domains of gait, chair transfer, and bed mobility.

Our most robust findings occurred at the functional level with respect to gait speed and ADLs. In subjects with PD, improvements in stride length, step cadence, gait initiation, walking velocity, and ADLs are consistently reported in the literature after participation in a rehabilitation program.[16,18,19,26,30,31] These studies all provide evidence supporting the functional gains that occur after PT intervention in the PD population. The literature on evidence-based practice supports functionally specific training as critical for progressing functional status.[32]

Interventions in the home environment and in the community, which more specifically address QOL issues, such as increasing socialization and participation in household and community activities, need further investigation. The impact of PT on the impairment level needs further clarification as well. In addition, the specific components of intervention that lead to the most profound changes are not well established. Most evidence supports the use of external cueing within the PT programs, but other critical ingredients are unclear and need

further investigation. Another key issue is related to determining optimal intensity of treatment. Studies consistently report PT programs offered during a span of 4 to 12 weeks, with sessions occurring 2 to 3 times a week. Several show gains in status at study completion, followed by a gradual decline and a return to baseline status between 3 to 6 months. In a multidisciplinary rehabilitation program for people with PD, Wade et al[33] showed short-term gains in mobility, with worsening disability at 6 months. Heterogeneity between groups related to medication adjustments and activity level may contribute to the lack of significant findings across outcome measures at the long-term follow-up assessment periods. It is worthy to consider, however, that perhaps people with a long-term chronic degenerative disease need intervention to occur over a longer time period. Instead of receiving a bout of exercise for a short period, they may need to continue the program for several months or more to maintain gains shown early on.

CONCLUSIONS

People with typical, idiopathic PD within Hoehn and Yahr stage II or III benefit in the short term from PT group treatment in addition to their MT with regard to function related to ADLs, CWS, and QOL related to mobility. Long-term benefits were observed in CWS, UPDRS ADL, and total scores but varied between groups.

Acknowledgments: We thank the physical therapists who implemented the rehabilitation program: Maureen Bourque, Lisa Azzam, Jean Peteet, Ingrid Burgers, Muriel Koolstra, and Nella Guinee; and those who assisted with data collection: Masa Kubo, Chia-ling Ho, Diane Dalton, Dan White, Paula McDonald, Samyra Keus, and Martijn Heijmans.

References

1. Booij J, Tissingh G, Winogrodzka A, van Royen EA. Imaging of the dopaminergic neurotransmission system using single-proton emission tomography and positron emission tomography in patients with parkinsonism. Eur J Nucl Med 1999;26:171-82.
2. Ng DC. Parkinson's disease. Diagnosis and treatment. West J Med 1996;165:234-40.
3. Tanner CM, Aston DA. Epidemiology of Parkinson's disease and akinetic syndromes. Curr Opin Neurol 2000;13:427-30.
4. Gleb DJ, Oliver E, Gilman S. Diagnostic criteria for Parkinson's disease. Arch Neurol 1999;56:33-9.
5. de Goede CJ, Keus SH, Kwakkel G, Wagenaar RC. The effects of physical therapy in Parkinson's disease: a research synthesis. Arch Phys Med Rehabil 2001;82:509-15.
6. Murphy S, Tickle-Degnen L. The effectiveness of occupational therapy-related treatments for persons with Parkinson's disease: a meta-analytic review. Am J Occup Ther 2000;55:385-92.
7. Deane KH, Jones D, Ellis-Hill C, Clarke CE, Playford ED, Ben-Shlomo Y. A comparison of physiotherapy techniques for patients with Parkinson's disease. Cochrane Database Syst Rev 2001;(1): CD002815.
8. Deane KH, Jones D, Playford ED, Ben-Shlomo Y, Clarke CE. Physiotherapy for patients with Parkinson's disease. Cochrane Database Syst Rev 2001;(3):CD002817.
9. McDowell I, Newell C. Measuring health: a guide to rating scales and questionnaires. New York: Oxford Univ Pr; 1996.
10. Kwakkel G, Wagenaar RC, Twisk JW, Lankhorst G, Koetsier JC. Intensity of leg and arm training after primary middle-cerebral-artery stroke: a randomised trial. Lancet 1999;354:191-6.
11. Post MW, De Bruin A, De Witte L, Schrijvers A. The SIP68: a measure of health-related functional status in rehabilitation medicine. Arch Phys Med Rehabil 1996;77:440-5.
12. Fahn S, Elton R. Unified Parkinson's Disease Rating Scale. In: Fahn S, Marsden CD, Calne D, Goldstein M, editors. Recent developments in Parkinson's disease. Vol 2. Florham Park: MacMillan Healthcare Information; 1987. p 153-63.
13. Comella CL, Stebbins GT, Brown-Toms N, Goetz CG. Physical therapy and Parkinson's disease: a controlled clinical trial. Neurology 1994;44:376-8.
14. Wagenaar RC, Van Emmerick RE. Resonant frequencies of arms and legs identify different walking patterns. J Biomech 2000;33: 853-61.
15. Wagenaar RC, Van Emmerik RE. Dynamics of pathological gait. Hum Mov Sci 1994;13:441-71.
16. Thaut MH, McIntosh GC, Rice RR, Miller RA, Rathbun J, Brault JM. Rhythmic auditory stimulation in gait training for Parkinson's disease patients. Mov Disord 1996;11:193-200.
17. Schenkman M, Cutson TM, Kuchibhatla M, et al. Exercise to improve spinal flexibility and function for people with Parkinson's disease: a randomized, controlled trial. J Am Geriatr Soc 1998;46:1207-16.
18. Scandalis TA, Bosak A, Berliner JC, Helman LL, Wells MR. Resistance training and gait function in patients with Parkinson's disease. Am J Phys Med Rehabil 2001;80:38-46.
19. Dam M, Tonin P, Casson S, et al. Effects of conventional and sensory-enhanced physiotherapy on disability of Parkinson's disease patients. Adv Neurol 1996;69:551-5.
20. Mohr B, Muller V, Mattes R, et al. Behavioral treatment of Parkinson's disease leads to improvement of motor skills and to tremor reduction. Behav Ther 1996;27:235-55.
21. Schenkman M, Morey M, Kuchibhatla M. Spinal flexibility and balance control among community-dwelling adults with and without Parkinson's disease. J Gerontol A Biol Sci Med Sci 2000;55:M441-5.
22. Protas EJ, Stanley RK, Jankovic J, MacNeill B. Cardiovascular and metabolic responses to upper and lower extremity exercise in men with idiopathic Parkinson's disease. Phys Ther 1996;76:34-40.
23. Hedges L, Olkin I. Statistical methods for meta-analysis. Orlando: Academic Pr; 1985.
24. Hoffer HM, Feiwell E, Perry R, Perry J, Bonnett C. Functional ambulation in patients with myelomeningocele. J Bone Joint Surg Am 1973;5:137-48.
25. Perry J, Garrett M, Gronley JK, Mulroy SJ. Classification of walking handicap in the stroke population. Stroke 1995;26:982-9.
26. Formisano R, Pratesi L, Modarelli FT, Bonifati V, Meco G. Rehabilitation and Parkinson's disease. Scand J Rehabil Med 1992;24:157-60.
27. Kamsma Y, Brouwer W, Lakke J. Training of compensation strategies for impaired gross motor skills in Parkinson's disease. Physiother Theory Pract 1995;11:209-29.
28. McIntosh GC, Brown SH, Rice RR, Thaut MH. Rhythmic auditory-motor facilitation of gait patterns in patients with Parkinson's disease. J Neurol Neurosurg Psychiatry 1997;62:22-6.
29. Nieuwboer A, De Weerdt W, Dom R, Truyen M, Janssens L, Kamsma Y. The effect of a home physiotherapy program for persons with Parkinson's disease. J Rehabil Med 2001;33:266-72.
30. Muller V, Mohr B, Rosin R, Pulvermuller F, Muller F, Birbaumer N. Short-term effects of behavioral treatment on movement initiation and postural control in Parkinson's disease: a controlled clinical study. Mov Disord 1997;12:306-14.
31. Szekely BC, Kosanovich NN, Sheppard W. Adjunctive treatment in Parkinson's disease: physical therapy and comprehensive group therapy. Rehabil Lit 1982;43:72-6.
32. Shumway-Cook A, Woollacott M. Motor control: theory and practical applications. Philadelphia: Williams & Wilkins; 1995.
33. Wade DT, Gage H, Owen C, Trend P, Grossmith C, Kaye J. Multidisciplinary rehabilitation for people with Parkinson's disease: a randomized controlled study. J Neurol Neurosurg Psychiatry 2003;74:158-62.

Supplier

a. SPSS Inc, 233 S Wacker Dr, 11th Fl, Chicago, IL 60606.