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Research Article

Comparing the Effectiveness of Vestibular Rehabilitation and Frenkel Exercise on Fatigue Reduction in Patients with Multiple Sclerosis: A Randomized Controlled Trial

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Abstract

Background: Fatigue is one of the most common complaints in people with Multiple Sclerosis (MS). The use of non-pharmacological interventions, such as exercise, may be effective in reducing fatigue in these patients.
Objectives: This study aimed to evaluate the effect of vestibular rehabilitation and Frenkel exercise on fatigue in patients with multiple sclerosis.
Methods: This study was a controlled randomized clinical trial. Seventy-five patients, who had medical records at the society of special diseases of the Yasuj University of Medical Sciences, Iran, in 2016, were randomly assigned to three groups, namely, vestibular rehabilitation, Frenkel, and control. The program lasted for 12 weeks (three sessions per week). Fatigue was measured by the Fatigue Impact Scale (FIS) before the intervention, and after that, at six and twelve weeks after the initiation of intervention.
Results: The mean score of fatigue in both experimental groups was decreased in a statistically significant manner after the end of the exercises, whereas it was increased in the control group. The reduction in fatigue was statistically significant in the vestibular rehabilitation exercise in comparison with the Frenkel exercise. The total fatigue in the vestibular rehabilitation group at six and twelve weeks after the intervention was -14.1 and -33.1, respectively, in comparison with before the interventions yet in the Frenkel group it was reported as -8 and -17.9, respectively. The comparison of the FIS subscales showed that there was a difference between the vestibular rehabilitation and Frenkel group in both the FIS physical ($P = 0.001$) and the psychosocial subscales ($P = 0.01$), yet no difference was observed between the two groups in the FIS cognitive subscale ($P = 0.1$) at twelve weeks after the intervention.
Conclusions: Both vestibular rehabilitation and Frenkel exercise could reduce fatigue in MS patients, however, vestibular rehabilitation was more effective compared to the Frenkel exercise in reducing fatigue.

Keywords: Exercise, Fatigue, Frenkel, Multiple Sclerosis, Rehabilitation, Vestibular

1. Background

Fatigue is defined as a decrease in physical and/or mental performance (1). It is one of the common complaints of patients with Multiple Sclerosis (MS). Seventy-four percent of such patients suffer from severe fatigue (2) and 80% experience fatigue in the first year of the onset of MS (3). Fatigue may be the result of hypothalamic-pituitary-adrenal axis changes, immune dysfunctions, and impaired nerve conduction (4). Fatigue can affect all aspects of quality of life (5) of MS patients.

Some medications, such as Amantadine, Levocarnitine, Glatiramer acetate (6), and Natalizumab (7) may be useful in reducing fatigue of MS patients; however, there are no known drugs with fewer side effects that can completely prevent or improve fatigue. Therefore, non-pharmacological interventions are considered as approaches for fatigue management (8). The review of the literature shows that biofeedback (9) and cognitive behavioral therapy (10) have been used to reduce fatigue in MS patients.

Exercise therapy is a non-pharmacological method, whose impact on MS symptoms has been investigated in previous studies (11, 12). It was previously thought that exercise leads to worsening of MS symptoms, in contrast, however, recent studies have revealed evidence to support that exercise is helpful for MS patients. Exercise can improve balance (13), mental functioning (14), and quality of life (15). Although the benefits of exercise are clear, some studies have shown that MS patients have a lower tendency to engage in an exercise in comparison with patients of other chronic diseases (16, 17). There is also no consensus about the effects of exercise therapy on fatigue in MS patients. Some studies have reported the positive effects of exercise on fatigue (18, 19); however, the ineffectiveness of exercise on fatigue has also been reported in some studies (20).

There are different therapeutic exercises, among which simple exercises, such as vestibular rehabilitation and Frenkel exercise, should be noted. Vestibular rehabilitation exercise compensates defects in the vestibular system via adaptation, habituation, and substitution (21), and thereby improves the performance of the cerebellar and visual system, and ultimately, the individual's balance (22). In one study, balance improvement was reported after patients with unilateral vestibular deficit underwent a vestibular rehabilitation exercise (23). Frenkel is a type of aerobic exercise that corrects motor defects in the cerebellum, stimulate voluntary movement control, and helps the Central Nervous System (CNS) compensate the loss of the kinesthetic sense or the body sensory information (knowing where it is in space) (24). It includes a series of slow, repetitious motions that are performed in different positions when lying down, sitting, and standing, and these programs target the cerebellum as the main center for controlling balance, and finally lead to an improvement in balance. In a case report study, the improvement of balance in a patient diagnosed with acquired immunodeficiency syndrome, associated with progressive multifocal leukoencephalopathy and neurotoxoplasmosis, was reported after a year of performing Frenkel exercise (25). Since fatigue is considered as the predictor of maintenance of somatic balance (26), it seems that patients, who attempt to maintain balance during the performance of tasks may experience significant levels of fatigue (27). Therefore, balance improvement, following these exercises, may be useful in reducing fatigue.

Since the prevalence of fatigue is high in MS patients and fatigue may be a sign of imbalance (28), and because of the lack of consensus on the impact of therapeutic exercises on fatigue, and the limitation of evidence indicating the effectiveness of intervention using vestibular rehabilitation and Frenkel exercise on fatigue in MS patients, further studies in this area are needed.

2. Objectives

The main question of this study is whether performing vestibular rehabilitation and Frenkel exercise could reduce fatigue as well as if there is any difference between the effectiveness of these exercises. This study was conducted to compare the effect of vestibular rehabilitation, and Frenkel exercise on fatigue in MS patients.

3. Methods

3.1. Patients

This study involved a controlled randomized clinical trial. The population of the study included MS patients, who had medical records at the Society of Special Diseases of Yasuj University of Medical Sciences, Iran, during the year 2016. The inclusion criteria for patients consisted of a confirmed diagnosis of disease by a neurologist, passing at least six months from the onset, being in the remission period, being between the ages of 15 and 55 years, ability to stand for 30 seconds, and to walk a distance of six meters without any assistance, to have a Fatigue Impact Scale (FIS) score from 54 to 107, no history of participation in a rehabilitation program within the last six months, and no diseases other than MS. Furthermore, the patients were evaluated by the Berg Balance Scale (BBS) to determine the existence of imbalance in these patients before the intervention. The patients, who had a BBS score from 21 to 40 or a moderate imbalance, were selected. Refusing to continue participation or inability to participate in exercises, and the relapse of diseases during the period of study were considered as exclusion criteria. Written informed consent was obtained before starting the exercises. Emphasis was placed on the confidentiality of information, and the patient's ability to exit at any stage during the study. The study was approved by the Research Ethics Committee of Yasuj University of Medical Sciences (ETH number: ir.yums.REC.1394.180), and was registered on site with the Iranian Registry Clinical Trials with IRCT, number; IRCT2016031527063N1 (29).

From the 120 available patients, a total of 75 eligible patients with multiple sclerosis, who met the inclusion criteria, were selected using the convenience sampling method and were allocated to two groups, vestibular rehabilitation, and Frenkel exercises, as well as a control group, based on block randomization. The sample size was calculated based on prior studies considering 95% confidence level, 80% power, $S_1 = 1.3$, $S_2 = 1.4$, and $\mu_1 - \mu_2 = 2.5$. The below formula was used:

$$n = \frac{2\left[\left(Z_{1-\frac{\alpha}{2}} + Z_{1-\beta}\right)\right]\left(S_1^2 + S_2^2\right)}{\left(\mu_1 - \mu_2\right)^2}$$

The randomization process was performed by a person, who was not involved in any part of the study procedure. The groups were randomly labeled (A = vestibular rehabilitation group, B = Frenkel group, and C = control group). Since there were three groups in this study, the total number of blocks was six in blocks of three. Random sampling with replacement was made from these blocks. During the intervention, one patient from the Frenkel exercise group dropped out due to disease relapse.

Furthermore, one patient from the vestibular rehabilitation group and one patient from the Frenkel exercise group dropped out of treatment due to being unable to regularly participate. There was no possibility of replacement because two months had passed since the starting of the exercises and due to the absence of another eligible sample. Finally, a total of 72 patients completed the study (Figure 1).

3.2. Procedure

Patients of both intervention groups had participated in exercise sessions that were held in the outpatient clinic of Shahid Beheshti Hospital during three exercise sessions, on alternate days, for a total span of 12 weeks. Each session lasted for about 60 minutes (Two 30-minute sessions with 15-minute rest intervals). The vestibular rehabilitation exercise was performed based on the protocols established by Cawthorne and Cooksey. On the basis of the aforementioned protocols, it was performed in both the sitting and the upright position; it was performed once with open eyes and then, the exercise was carried out with closed eyes (30, 31). The protocol is described in details in Appendix 1 in Supplementary File.

Patients in the Frenkel group performed exercises based on protocols obtained from a previous study (32). Frenkel exercise was performed in the following different positions, including lying down, sitting up, and standing (Appendix 2 in Supplementary File for details). Patients in the control group only received routine care.

3.3. Measures

Patients' fatigue was assessed by the Fatigue Impact Scale (FIS) before the exercises, six and twelve weeks after the start of exercises. The FIS was designed by Fisk et al. to assess fatigue in MS patients (33). This scale contains 40 items, and assesses the functional limitations of people in subscales of categories: Cognitive (10 items), physical (10 items), and psychosocial (20 items). Items of the cognitive subscale measure concentration, memory, thinking, and the organization of thoughts. The physical subscale reflects a person's motivation, effort, tolerance, and harmony. The psychosocial subscale evaluates the impact of fatigue upon isolation, emotions, workload, and coping. Items are rated on a five-point Likert scale. Each item is graded from zero (no problem) to four (extreme problem), and the range of the total fatigue score is 0 to 160. The validity and the reliability of the Persian version of FIS have been confirmed previously (34).

3.4. Data Analysis

The collected data were analyzed using descriptive and inferential statistics, employing the IBM SPSS Statistics Software for Windows, version 19.0 (IBM Corp., Armork, N.Y. USA) by considering a confidence interval of 95%. At first, the distribution of fatigue was assessed by the Kolmogorov-Smirnov *Z*-test. It had a normal distribution, therefore, the results of the parametric tests were reported for analysis. A Repeated-Measure Analysis of Variance (ANOVA) was used to compare the mean score of fatigue among the three groups. Since the assumption of Mauchly's test of sphericity of repeated measures ANOVA test was violated, Greenhouse Geisser epsilon correction was reported. The mean difference of fatigue was significant; therefore, pairwise comparison of the mean difference was conducted by Bonferroni post hoc test. Because there were three groups in this study, the significance level was equal to or less than 0.015 ($\alpha/3$) in the pairwise comparison.

4. Results

Seventy-two patients aged between 18 and 48 years (Mean: 32.7 $\pm$ 7.4) participated in this study. About 56 (77.8%) patients were female, 68 (94.4%) patients had the relapsing-remitting type of MS, and four (5.6 %) patients had primary and secondary progressive type of MS. Forty-two (58.4%) patients used the interferon Beta-1a drug, 16 patients (22.2%) used the interferon Beta-1b, and the other patients used other drugs. The mean body mass index, the age of disease onset, and the duration of illness were 23.4 $\pm$ 2.3 kg/m^2, 27.6 $\pm$ 7.2 years, and 60.5 $\pm$ 37.4 months, respectively. No statistically significant difference was observed among the three groups by the demographic variables ($P = 0.7$).

Repeated measures ANOVA test showed statistically significant differences in the mean the total fatigue scores and its subscales in terms of time/group among the three groups ($P < 0.05$) (Table 1). Pairwise comparison of the mean difference of the total fatigue and its subscales scores showed that there were statistically significant differences between the three groups at the baseline and six weeks after starting the intervention ($P > 0.05$), except in case of vestibular rehabilitation and in the control group, in which pair-wise comparison for six weeks post-intervention was significant ($P = 0.009$). A statistically significant difference was observed between the vestibular rehabilitation and the Frenkel groups at the end of the intervention ($P = 0.007$). Comparing the FIS subscales between the vestibular rehabilitation and the Frenkel groups

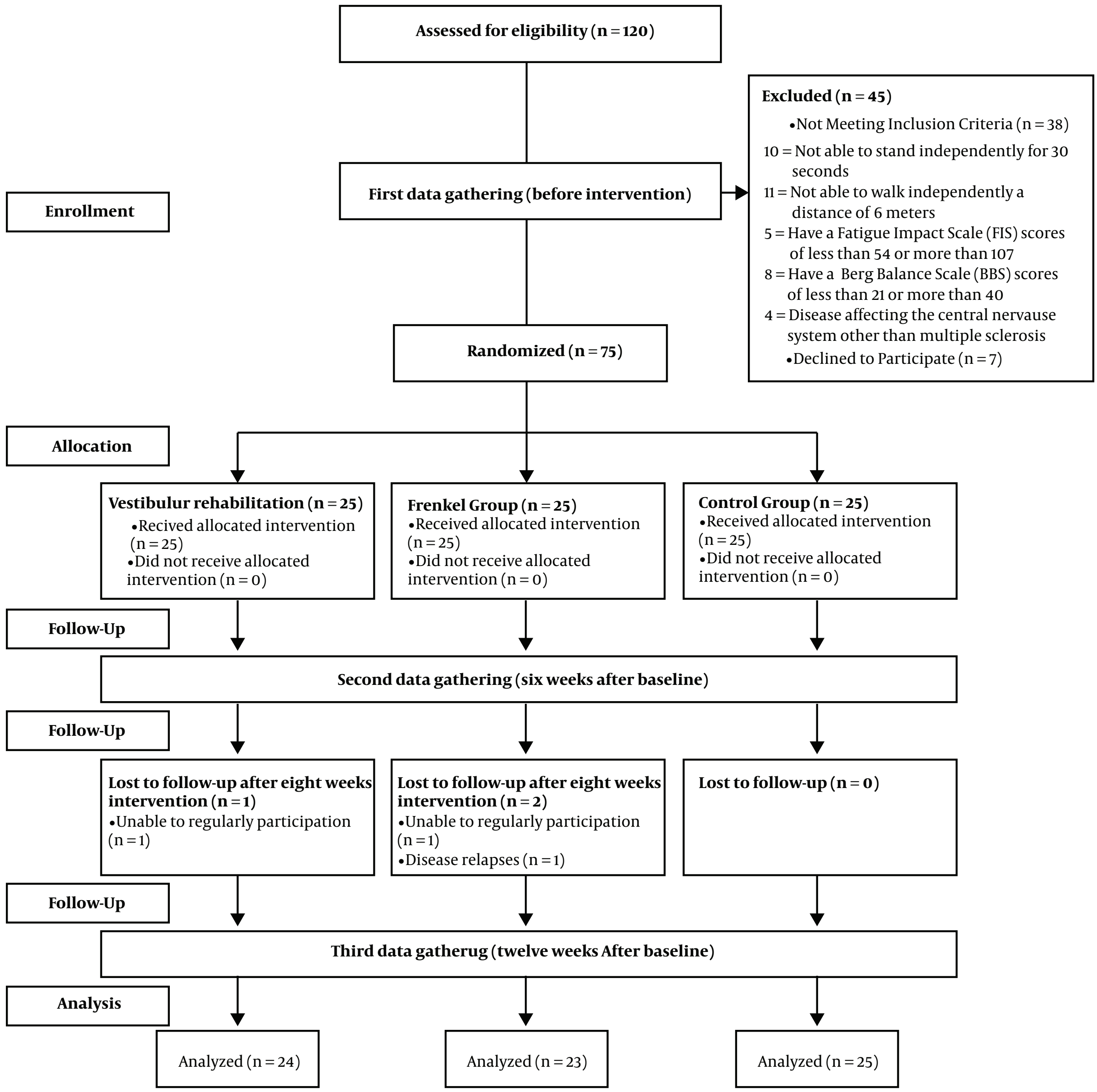

Figure 1. The study design

showed that there was no difference in the cognitive subscale (P = 0.1); significant differences were, however, observed by the physical (P = 0.001) and the psychosocial subscales (P = 0.01) at the end of the intervention (Table 2).

There was a statistically significant reduction in the mean score of total fatigue of the two exercise groups; in other words, both interventions reduced fatigue in the patients. However, the reduction of fatigue was statistically significant in vestibular rehabilitation exercise in comparison with Frenkel exercise. The mean total fatigue in the vestibular rehabilitation group was 92.7 ± 12.8, 78.2 ± 15.2, and 63.4 ± 14.6, respectively, before the interventions, and six and twelve weeks after it; also, in the Frenkel group, the mean fatigue at these aforementioned times was 89.6 ± 16.4, 84.3 ± 16.6, and 78.6 ± 16.3, respectively. Fatigue was not reduced in the control group, and it gradually increased according to the FIS score from 89.2 ± 15.5 at baseline to 96.5 ± 18 at the end of the study.

Furthermore, a difference in the mean scores of total fatigue was observed in both the vestibular rehabilitation and the Frenkel group in comparison with the control group, at the end of the intervention (P = 0.001). The differences in the mean scores of total fatigue in the vestibular rehabilitation group in comparison with the control group, six and twelve weeks after intervention, were 14.1, and 33.1, respectively; in the Frenkel group, however, the differences were 8 and 17.9, respectively.

Additionally, the findings showed that there was a balance in the improvement of exercise groups after the intervention (P = 0.001). Therefore, correlational analyses were performed to test the relationship between fatigue and balance. The Pearson correlation coefficient test was used for the analysis of associations; a negative correlation between fatigue and balance was reported at the end of the intervention phase (r = -0.5, P < 0.001).

5. Discussion

The effectiveness of vestibular rehabilitation and Frenkel exercise on fatigue were compared among MS patients in the present study. The results showed that fatigue decreased in MS patients following the mentioned exercises and the vestibular rehabilitation exercise was more effective in decreasing fatigue in comparison to the Frenkel exercise.

Consistent with available studies about the effectiveness of exercise therapy, Kierkegaard et al. (35), and Giesser (36) reported reduced fatigue in MS patients following different exercise therapies. How exercises decrease fatigue in MS patients is still poorly understood, however, the reason behind this decrease may be due to the effect of exercises in increasing energy reserves and enhancing neurobiological processes (37). In addition, environmental physiology changes, such as increasing oxygen and blood supply to muscles that occur after exercise, may be effective in reducing fatigue (38). In contrast to the current findings, a study by Pilutti et al. showed that supported treadmill training had a low impact on decreasing fatigue in MS patients (39). Furthermore, Newman et al. found that the level of fatigue in MS patients was unchanged after aerobic training (40). Results contradicting the aforementioned phenomenon may be due to the type and the duration of exercises, methodology of the studies, and the various fatigue assessment tools.

Patients in the current study experienced a reduction in fatigue following both exercise programs in comparison to the control group. The reason for this finding may be due to the effect of these exercises on improving the patient's balance; therefore, they can reduce fatigue. As in this study, there was a correlation between increasing balance and decreasing fatigue. The effect of vestibular rehabilitation exercise on improving various symptoms, such as dizziness, quality of life (41), and balance (42) in MS patients and also reducing the risk of falls in older adults (43) have been reported. On the other hand, the positive effect of Frenkel exercise for elderly individuals as well as for patients with neurological disorders associated with imbalances was reported in a study by Makuła (44). Increasing fatigue in the control group of the current study indicated that the lack of a planned exercise program may lead to worsening of symptoms in patients with MS. The other result of the current study showed that vestibular rehabilitation exercise was more effective than Frenkel exercise. This finding had a number of similarities with the results of Hebert et al., they showed that MS patients, who participated in vestibular rehabilitation exercise experienced decreased fatigue than the exercise control group and the wait listed control group (45). Vestibular rehabilitation exercises can affect three balance centers (i.e. the cerebellum, vestibular, and the visual system) at the same time (46, 47). This can result in improving balance, and subsequently, further fatigue reduction. Frenkel exercise may only improve the cerebellum function for coordinating movements (48).

According to another finding of the current study, there were differences in the reductions of fatigue in the physical and psychosocial subscales between the two exercises, yet no difference was observed in the cognitive subscale. The treatment of cognitive fatigue is very complex as a variety of factors may be involved in its origin (49), and it has a negative effect on cognitive tasks, physical conditions, and social functions (50). Therefore, treatments should target to improve cognitive fatigue in MS patients.

Although the findings of this study are related to the positive effects of vestibular rehabilitation and Frenkel exercise on fatigue in MS patients, some limitations need to be considered. The first limitation was the data collection tool. Although the reliability and the validity of the FIS has been approved in Persian, being a self-report questionnaire in addition to the subjective nature of fatigue might have an influence on the accuracy of patients to answer questions. Therefore, further studies are suggested to examine the effectiveness of these exercises with other fatigue measures, particularly with more objective tools. The second limitation of this study was that the majority of patients in this study had the relapsing-remitting type of MS. Since fatigue may be different in the four types of MS (relapsing-remitting, secondary-progressive, primary-progressive, and progressive-relapsing), further studies are recommended to investigate the effects of the mentioned exercises on fatigue in MS patients with the other forms of the disease.

In summary, the current study showed that both vestibular rehabilitation and Frenkel exercise could reduce fatigue at the end of the exercises, however, there were significant differences in the effects of these exercises. In other words, the vestibular rehabilitation exercise is more effective than the Frenkel exercise in reducing fatigue. Finally, the researchers suggest that these exercises should be performed alongside medication in MS patients owing to their various benefits, such as ease of learning, low cost, and non-invasive nature.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

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Footnotes

Authors' Contribution: Fatemeh Karami: designing the research, sampling, allocating samples to the study groups, implementation of the intervention, collecting data, and compiling the article; Ardashir Afrasiabifar: monitoring of intervention, analysis of data, and compiling the article, and Shahla Najafi Doulatabad: collecting data.

Conflict of Interests: None declared.

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Table 1. Between Group Comparisons of Mean Scores of Patients' Fatigue[a]

Fatigue/Times	Vestibular Rehabilitation Group				Frenkel Group				Control Group				P Value (Time/Group)
	Mean ± SD	Change Scores from Baseline, Mean (SD)	95% Confidence Interval for Mean		Mean ± SD	Change Scores from Baseline, Mean (SD)	95% Confidence Interval for Mean		Mean ± SD	Change Scores from Baseline, Mean (SD)	95% Confidence Interval for Mean		Repeated Measures ANOVA
			Lower Bound	Upper Bound			Lower Bound	Upper Bound			Lower Bound	Upper Bound	
Total fatigue													0.001
T1	92.7 ± 12.8	-	86.6	98.8	89.6 ± 16.4	-	83.4	95.8	89.2 ± 15.5	-	83.2	95.1	
T2	78.2 ± 15.2	-14.5 (3.4)	71.6	84.8	84.3 ± 16.6	-5.3 (2.4)	77.6	91	92.3 ± 16.5	3.1 (2.2)	85.9	98.8	
T3	63.4 ± 14.6	-29.3 (4.30	56.8	70.1	78.6 ± 16.3	-11 (2.1)	71.7	85.4	96.5 ± 18	7.3 (4.5)	90	103.1	
Cognitive subscale													0.001
T1	20.4 ± 3.5	-	18.8	21.9	22.5 ± 4.1	-	20.9	24.1	19.7 ± 4	-	18.2	21.3	
T2	18.7 ± 3.3	-1.7 (1.4)	17.4	20.1	20.2 ± 3.5	-2.3 (1.4)	18.8	21.6	20.8 ± 3.6	1.1 (1.3)	19.5	22.2	
T3	16.3 ± 3.4	-4.1 (2.2)	14.8	17.7	17.9 ± 3.6	-4.6 (1.9)	16.4	19.4	22 ± 3.6	2.3 (1.9)	20.5	23.4	
Physical subscale													0.01
T1	28.3 ± 4.8	-	26	30.7	27.8 ± 5.5	-	25.4	30.2	26.6 ± 6.9	-	24.3	29	
T2	21.2 ± 4.7	-7.1 (2.4)	18.9	23.6	25.9 ± 5.3	-1.9 (1.7)	23.5	28.3	27.4 ± 6.7	0.8 (1.1)	25.1	29.7	
T3	14.4 ± 4.6	-13.9 (2.7)	12.3	16.6	23.8 ± 4.5	-4 (1.9)	21.6	26	28.8 ± 6.4	2.2 (1.7)	26.7	30.9	
Psychosocial subscale													0.001
T1	44 ± 9.7	-	39.7	48.3	39.3 ± 11.5	-	34.9	43.6	42.8 ± 10.1	-	38.6	47	
T2	38.2 ± 10	-5.8 (2.3)	33.9	42.5	38.2 ± 11.3	-1.1 (1.2)	33.7	42.6	44.1 ± 10.7	1.3 (1.2)	39.8	48.3	
T3	27.9 ± 6.6	-16.1 (3.8)	23.8	32.1	36.9 ± 11.3	-2.4 (1.3)	32.7	41.1	45.8 ± 11.5	3 (2.4)	41.7	49.8	

[a] T1, baseline; T2, six weeks after starting the intervention; T3, twelve weeks after starting the intervention.

Table 2. Paired Comparison of the Mean Differences of Patients' Fatigue by Time/Group

Fatigue/Times	Paired Comparison											
	Vestibular Rehabilitation-Frenkel				Vestibular Rehabilitation-Control				Frenkel-Control			
	Mean Difference	95% CI for Mean Difference		P Value[a]	Mean Difference	95% CI for Mean Difference		P Value[a]	Mean Difference	95% CI for Mean Difference		P Value[a]
		Lower Bound	Upper Bound			Lower Bound	Upper Bound			Lower Bound	Upper Bound	
Total fatigue												
T2	-6.1	-17.6	5.4	0.4	-14.1	-25.4	2.8	0.009	-8	-19.4	3.4	0.2
T3	-15.2	-26.8	-3.4	0.007	-33.1	-44.6	-21.6	0.001	-17.9	-29.6	-6.3	0.001
Cognitive subscale												
T2	-1.5	-3.9	1	0.1	-2.1	-4.5	0.3	0.09	-0.6	-3.1	1.8	0.8
T3	-1.6	-4.2	0.9	0.1	-5.7	-8.1	-3.2	0.001	-4.1	-6.6	-1.5	
Physical subscale												
T2	-4.7	-8.7	-0.6	0.01	-6.2	-10.1	-2.1	0.001	-1.5	-5.5	2.5	0.6
T3	-9.4	-13.1	-5.5	0.001	-14.4	-18	-10.6	0.001	-5	-8.8	-1.3	0.005
Psychosocial subscale												
T2	0	-7.6	7.6	0.9	-5.9	-13.3	1.6	0.1	-5.9	-13.5	1.7	0.1
T3	-9	-16.1	-1.7	0.01	-17.9	-24.9	-10.7	0.001	-8.9	-16	-1.7	0.009

Abbreviation: CI, confidence interval.
[a] Post Hoc.