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Effects of Multicomponent Exercise Training Program on Biochemical and Motor Functions in Patients with Alzheimer's Dementia

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Abstract: The aim of this study was to examine the effects of a multicomponent exercise training program on motor function and biochemical markers in patients with Alzheimer's-type dementia. Twenty patients with Alzheimer disease, divided into the intervention group (IG; aged 84 $\pm$ 3.1 years) and the control group (CG; aged 86 $\pm$ 2.6 years) were included in this study. The intervention group was enrolled into an exercise training program for three months (two sessions of 60 min per week). The CG was instructed to follow their daily rhythm of life (e.g., rest, reading) without a physical training program. After 3 months of participation in a multicomponent exercise program, gait speed, balance and walking parameters were all improved in the intervention group as measured with the Berg Balance Scale, the Tinetti test, the 6-min walking test and the timed up and go test ($p < 0.05$ for all; percentage range of improvements: 3.17% to 53.40%), except the walking while talking test, and biochemical parameters were not affected ($p > 0.05$). Our results demonstrate that exercise improves postural control, aerobic capacity and mobility functions in patients with Alzheimer disease. Physical exercise is a safe and effective method for treating physical disorders in patients with Alzheimer's disease and can easily be integrated in various programs for the management of Alzheimer disease.

Keywords: Alzheimer's disease; physical exercise; motor function; lipid profile; aerobic capacity; older

1. Introduction

Alzheimer disease is a progressive neurodegenerative disorder that accounts for the major cause in dementia worldwide [1]. Genetic and environmental factors contribute to the development of the disease, which is progressive and irreversible and results in cognitive and motor functions impairments [2]. The number of disease cases is expected to reach 106.8 million worldwide by the year 2050 [3]; the progression of this alarming number can be explained by the fact that the main risk factor for this neurodegenerative disease is age [4]. Currently, there is no definitive cure for Alzheimer disease; researchers in this specific area are exploring preventive therapeutic strategies that could control the progression of the disease [5]. During the last 10 years, it has been reported that physical activity has a beneficial impact and constitutes an effective solution for neurodegenerative diseases such as Alzheimer disease [6]. Prevention of Alzheimer disease can be pharmacological, non-pharmacological or a combination of both. At present, medications such as cholinesterase inhibitors and memantine produce limited benefits and do not convincingly reduce Alzheimer severity by retarding cognitive and functional decline [7]. Therefore, interest in non-pharmacological treatments for combating Alzheimer disease is increasing [8,9]. Thus, a great amount of effort and research have been undertaken to understand the physiology of the aging brain, which is changed by the type of physical activity [10]. A potent non-pharmacological treatment is physical activity, which is both known to improve cognitive function and reduce risk of cognitive decline and dementia [11]. Physical exercise is a powerful instrument used to limit the physical and functional impairments in patients with Alzheimer disease [12]. Recent studies have emphasized the impact of physical inactivity on the increased risk of developing neurodegenerative disease [13] and most particularly Alzheimer's disease [14]. According to the American College of Sports Medicine (ACSM) [15], physical exercise contributes to reducing and to delaying the progression of chronic disease, including those associated with the aging process and related to cognitive and motor disorders. However, several studies reported the beneficial impacts of exercise as a preventive measure against Alzheimer's disease [16].

Physical exercise interventions have been shown to be beneficial in patients with cognitive disorders [17] and delay the progress of the chronic disease [18]. At present, we know that physical exercise decreases the gravity of cognitive impairments in older patients with Alzheimer's disease [19] and has many beneficial effects, improving physical condition, increasing autonomy and improving life quality in patients with neurodegenerative disease [20]. Research findings show evidence for different factors, such as type of exercise, frequency, intensity, time and the total duration of intervention follow-up [18]. In addition, pharmacological treatments fail to examine the cause of Alzheimer disease, and only a few symptomatic treatments are available with side effects such as weight loss and nausea [21]. Physical exercise has shown more positive results concerning chronic disease conditions [22]. For people with Alzheimer's disease, there are several benefits for traditional cardiovascular risk factors, such as the reduced vascular flow and diabetes, which are involved in the pathogenesis of this disease [19]. It is quite important that patients maintain a physical training program for a prolonged period to obtain more beneficial effects [23]; even a minimal level of exercise (e.g., walking) generates some health benefits, as opposed to being sedentary [24].

The cognitive benefits of physical activity in patients with Alzheimer disease have been widely examined [25,26], with physical activity exerting a beneficial neuroprotective impact, reducing the incidence of mild cognitive impairment and delaying the onset of dementia [27]. Furthermore, physical activity at midlife appears to exert a neuroprotective effect later in life. For example, physical activity twice a week appears to reduce the prevalence of dementia and Alzheimer by half, two decades later [28,29]. In additional to neuroprotection, physical activity could improve functional ability in people with Alzheimer disease. For example, a physical exercise program (30 min of moderate-intensity exercise per day) has been demonstrated to improve the physical and emotional health of patients with Alzheimer [30]. Moreover, Kemoun et al. [31] confirmed the beneficial effect of exercise on physical and cognitive abilities by reporting improved cognitive function and walking speed in people with Alzheimer after 19 weeks of exercise.

The biochemical benefit of exercise in disease states is widely researched. This includes reduced oxidative stress in obese patients [32], improved glucose homeostasis in diabetes mellitus [33] and reduced low-grade inflammation in coronary artery disease [10]. Most research on patients with Alzheimer disease understandably concerns the influence of exercise on neurotrophic biomarkers.

For example, exercise alters beta-amyloid pathology in a rodent model of Alzheimer [34,35]. Moreover, the brain-derived neurotrophic factor, which ensures growth and survival of neurons, is increased following exercise training in mice [36].

However, there is a paucity of data concerning the biochemical effect of physical activity on biomarkers related to lipid profile, glucose homeostasis and organ function in Alzheimer patients. As such, more data are required from randomized controlled trials in humans to understand the biochemical and functional ability effects of exercise in Alzheimer patients. Therefore, the primary objective of this investigation was to examine the effect of exercise training on balance, walking speed and postural stability in elderly patients with dementia. Furthermore, changes in biomarkers associated with lipid profile, renal function and liver function were assessed. We hypothesized that an exercise training program would be an effective treatment for patients with Alzheimer's disease.

2. Materials and Methods

2.1. Participants

Twenty elderly participants were recruited (aged 85 ± 3 years, with a body mass index of 26.3 ± 1.5 kg/m^2 and an average Mini-Mental State Examination [MMSE] score of 19.38 ± 1.20). Most were female (n = 14); 7 drank alcohol, 6 were smokers and 18 presented comorbidities (Table 1). Subjects were informed about the experimental procedure and subsequently signed a written consent form according to the standards of the Committee for Protection of Persons of the University of Monastir (Tunisia). Patients were diagnosed with Alzheimer disease according to the International Working Group diagnosis criteria (IGW) [37] at the Neurology department of Monastir Hospital. We only recruited patients with early and moderate-stage Alzheimer disease (Clinical Dementia Rating (CDR) of 0.5 or 1 (very mild to mild dementia), who had the full capacity to consent [38].

Table 1. Characteristics of the Alzheimer's patients in a control and intervention group.

Characteristics	Overall Population	Control Group	Intervention Group
Patients (N)	20	9	11
Years	84 ± 3.0	86 ± 2.6	84 ± 3.1
Body Mass Index (kg/m^2)	26 ± 1.5	25 ± 1.3	27 ± 1.1
Higher education level	15	7	8
Alcohol use	7	3	4
Comorbidities	18	8	10

The following criteria for inclusion were: Mini-Mental State Examination [MMSE] [39] score between 12 and 20; aged 65 or older; having normal or corrected-to-normal vision and colour perception; no drug treatment during the training protocol; living in medical care environment; and able to walk without technical assistance. None of the participants were excluded from the study due to reporting an MMSE score below 12 (indicating severe dementia and impairment); this test was used to examine the degree of cognitive level before starting the physical training program. Patients with clinically relevant medical conditions, e.g., heart disease, hypertension or diabetes or a medication that could influence cognitive functioning (e.g., benzodiazepines, sleep aids, neuroleptics) were excluded from study participation.

Eligible participants were randomly allocated to two groups. The first group of nine patients served as the control whilst the second group of eleven patients underwent physical training for three months, twice per week (60 min per session). Both groups underwent the same five tests in the morning, pre- and post-intervention period.

2.2. Mini-Mental State Examination (MMSE)

The MMSE is the most widely used brief screening measure for dementia [39]. Administration takes 5–10 min, and the following domains are evaluated: concentration or working memory; language and praxis; orientation; memory; and attention span. A total of 30 points is possible, and a score below 24 was originally identified as a threshold for cognitive impairment during validation of MMSE. A score <24 is generally considered a threshold for "mild dementia", 19–24 indicate "moderate dementia" and 10–18 indicate "severe dementia" <10 [39].

2.3. Tinetti Test

The Tinetti balance subscale [40], which has demonstrated reasonable reliability and validity [41], involves rating individuals on 13 common tasks. It is a tool to assess abnormalities in balance and the gait of elderly subjects in various situations of everyday life [42]. The total possible score is 16, with higher scores indicating better performance.

2.4. The Berg Balance Scale

The Berg Balance Scale is the best-known balance measurement tool that accesses balance and functional activities, such as reaching, transferring, bending and standing in patients with physical and motor impairments. It consists of qualitative measures in postural control capacity: sitting and transferring oneself safely between two chairs; standing with one foot apart, two feet together, in single-leg stance and feet in the tandem Romberg position with both with eyes open and closed; standing and reaching down to pick up an object from the floor. Each item is scored according to a 5-point scale, ranging from 0 to 4 (in which 0 indicates the lowest level of function and 4 indicates the highest level of function). The total possible score is 56 points, and 41–56 suggests a low fall risk, 21–40 a medium fall risk and 0–20 a high fall risk. A change of 8 points between two assessments indicates a clinically meaningful change in function [42].

2.5. Six-Minute Walking Test (6MWT)

The six-minute walk test has been used to evaluate aerobic capacity in functional exercise performance [43]. It is a safe, simple and easy diagnostic test for evaluating motor capacity [44] in older patients [45] with cognitive and intellectual disorders [46]. This test consists of measuring the greatest possible distance that a subject can travel on a flat surface in 6 min without running. The participant walks at a comfortable rhythm for 30 m across a covered, flat, rectilinear distance, which is well-defined and not frequented. It is marked every 3 m, and two cones mark the place of U-turns. A coloured band is used to mark the starting line. This test has been widely used for measuring functional parameters in older patients [47].

2.6. Timed up and Go Test

The timed up and go test is a test that quantitatively assesses mobility and static and dynamic balance. A chair with armrests, a stopwatch/wristwatch and a tape to mark 3 m are needed for the measurement, which represents the time taken to rise from the chair, walk 3 m, turn around, walk back and sit down. A value of >14 s indicates a high fall risk [48].

2.7. The Walking and Talking Test (WTT)

This test involves the so-called dual-task paradigm, and it is a strong predictor of fall risk. Patients start walking on a computerized mat surface while reciting alternate letters of the alphabet in two different conditions. Subjects are then asked by the tester to concentrate and pay attention in both walking and talking tasks. Then, patients are asked to recite alternate letters and not to focus on the walk. Participants perform two trials, each under a different condition. Patients may slow down during the test execution if they need to stop and think about the next letter. Patients may start walking again as soon as they can. No encouragement for the patients was given, and testers intervened only in urgent situations. In the case of the latter, the trial was not recorded, and patients started a new one. Letters varied randomly between "A" (A-C-E) and "B" (B-D-F) between each trial. To reduce and limit the learning impact, patients were given more practice trials as required for both the single and dual-task conditions to familiarize themselves with the procedure of the test. The tester recorded the total number of alternate letters correctly recited in sequence and the total number of errors for 2 trials during each condition. If subjects made an error but continued accurately, the total number of alternate letters correctly recited was counted [49].

2.8. Blood Analysis and Biomechanical Assays

All blood samples were collected between 09 h:00 and 11 h:00. Following an overnight fast, participants rested in a seated position for 15 min to measure blood pressure (Omron Model HEM-737AC, Omron Healthcare, Inc., Vernon Hills, IL, USA) [50]. Five minutes later, the resting blood sample (10 mL) was collected in serum separator tubes. Samples clotted before being centrifuged at 4000 rpm for 20 min at 4 °C and were then analyzed with an automated analyzer (KBio 2 Kitvia, Labarthe-Inard, France) operating on the principle of liquid chemistry to measure NFS parameters. Lipid profile (triglycerides and cholesterol), renal function (creatinine), liver function (alanine aminotransferase [ALT]), aspartate aminotransferase (AST), alkaline phosphatase and total bilirubin, urea, calcium (Ca), glucose, potassium (K) and sodium (Na) were quantified in duplicate.

2.9. Multicomponent Exercise Training Program

The posture–balance–motility (PBM) program is an animation tool for people with a loss of autonomy. It has the objective of improving the quality of life through a bio–psycho–social approach based on adapted and individualized physical activity as a support for mobilizing the skills of the elderly person [51]. This program consists of three types of exercises: mobility, posture and balance. In the present investigation, the posture–balance–mobility program ran for 3 months (12 weeks) with two sessions per week of one hour each: 10 min of warm-up (walking on a treadmill at 3 km/h^{-1}), 20 min of walking, muscle building and joint movement, 20 min of balance and posture training and 10 min of stretching. The first main 20 min was based on walking exercises to improve postural parameters with motor athletic parkour with 30 m of walking distance; the parkour was composed of three lines 10 m apart, indicated with six differently coloured cones: two red cones indicated the first 10 m, two blue cones were used for the second line and two yellow cones for the final line. Participants were encouraged to walk the entire distance of the three lines, touching the two cones of each line. The second main 20 min was based on mini golf exercises, in which participants practiced static and dynamic balance exercises with low-to-moderate intensity. We encouraged caregivers to play with their patients sometimes, and this was helpful and motivational. Before starting the exercises, 20 min were needed to make sure that the patients were in a resting position and dressed in comfortable clothes. The presence of relative partners or caregivers is essential to assist and support patients during all the activities.

2.10. Statistical Analysis

Data were visually inspected for potential outliers, and normality was checked using the Shapiro–Wilk test due to the small sample size. Based on the normal distribution, parametric tests were used. Chi-squared test, Student's *t*-test and repeated-measures analysis of variance (ANOVA) with Bonferroni's post hoc test were conducted to test for an effect of group (control and intervention) and time (pre- and post-training). The reliability of the variables in this study was determined using Cronbach's alpha. All statistical analyses were carried out using the commercial software Statistical package for social sciences (SPSS version 23.0, IBM, Chicago, IL, USA). The alpha level was set a priori at $p < 0.05$.

3. Results

3.1. Change in Physical Function

Table 2 presents the comparison within and between groups at baseline and post-intervention for all performance parameters.

Table 2. Performance parameters in Alzheimer's patients in a control and intervention group pre-and post-intervention.

Variable	Control Group		Delta Change (%)	Intervention Group		Delta Change (%)	*p*-Value		
	Before	After		Before	After		Group	Time	Interaction
Berg Balance Scale	42.22 ± 2.68	41.00 ± 1.73 *	2.8	41.92 ±2.78	43.25 ± 2.14 *	3.17	0.306	0.914	0.021
Tinetti test	12.67 ± 2.24	13.56 ± 0.88 *	7.02	12.17 ± 1.80	18.67 ± 1.07 *	53.40	<0.001	<0.001	<0.001
6-min walking test	115.89 ± 9.53	150.67 ± 14.38 *	30.01	111.00 ± 21.39	169.33 ± 16.51 *	52.50	0.273	<0.001	0.008
Time up and go	21.78 ± 2.82	23.33 ± 1.66 *	7.11	23.50 ± 3.48	20.08 ± 1.51 *	−14.50	0.425	0.141	0.001
Walking and Talking	0.56 ± 0.53	0.56 ± 0.53	0	0.58 ± 0.67	1.25 ± 0.62 *	115%	<0.001	<0.001	<0.001

* indicates a significant increase from pre- to post-test for this group with $p < 0.05$.

At baseline, there were no differences between groups. In addition, the intervention group improved in most of the physical tests after 3 months of participating in the physical activity program. However, after training, the exercise group achieved a significantly better performance in balance and postural capacity. For the Tinetti test (TT), there was an effect of group, time and interaction ($p < 0.001$); patients were able to realize all the 13 subtests, and they achieved a better performance in TT than the control group (IG = 53.4%; CG = 7.2%). The interrater reliability values of the Tinetti test's Cronbach alpha were 0.97 (0.94–0.98) and 0.94 (0.90–0.97) for both balance and gait subscales (Figure 1).

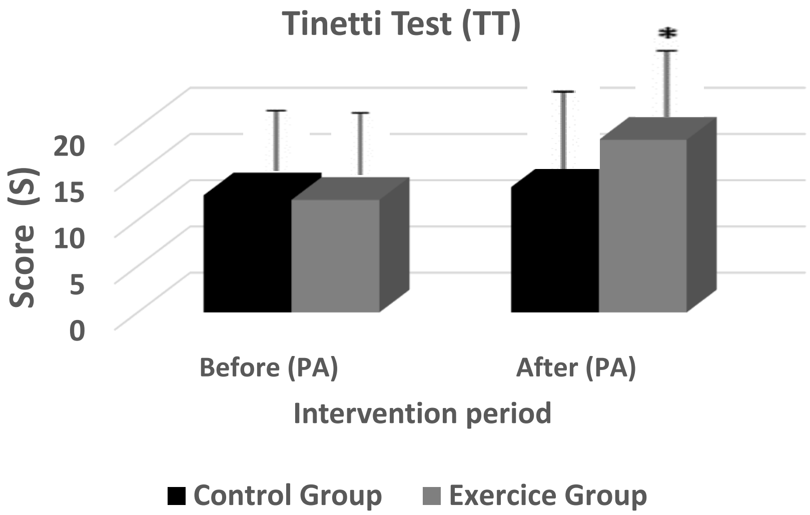

Figure 1. Tinetti test comparisons within and between groups at baseline and post-intervention. Values are means (±SD). * Significantly different ($p < 0.05$) for the intervention group after 12 weeks of multicomponent physical training program.

In the 6MWT, patients in the exercise group walked a longer distance in comparison with the baseline measure, a significant improvement in walking distance with less stability disorders and time ($p < 0.001$), and the interaction (group × time; $p = 0.008$) reached significance, where the intervention group improved more than the control group IG = 52.5%; CG = 30.1% (Figure 2).

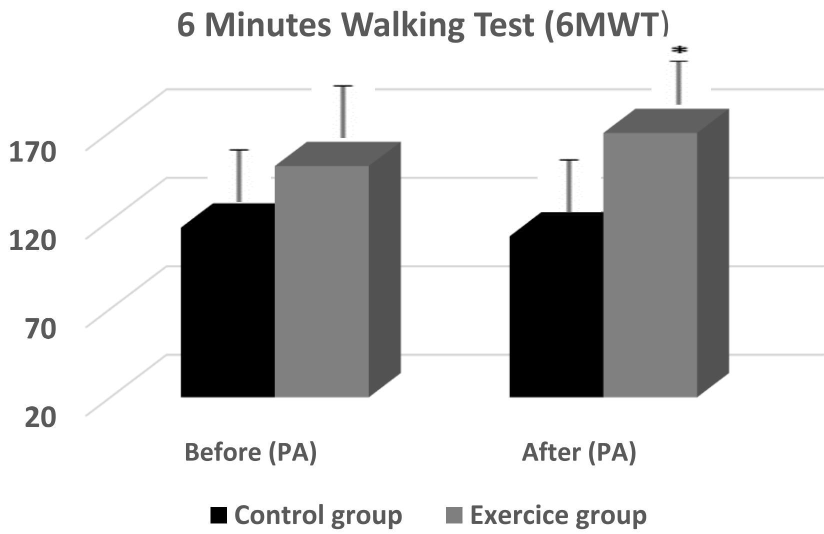

Figure 2. Six-Minutes Walking test comparisons within and between groups at baseline and post-intervention. Values are means (±SD). * Significantly different ($p < 0.05$) for the intervention group after 12 weeks of multicomponent physical training program.

Performance in the Berg Balance Scale improved significantly after the intervention protocol ($p = 0.001$). The improvements of the score in static and dynamic balance abilities in patients with Alzheimer's disease with a better result in the intervention group were IG = 3.17%; CG = 2.8%. The interrater reliability values of the balance scale score with global ratings of the patients ranged from 0.47 to 0.51 and from 0.39 to 0.45. The coefficients were moderate and statically significant (Figure 3).

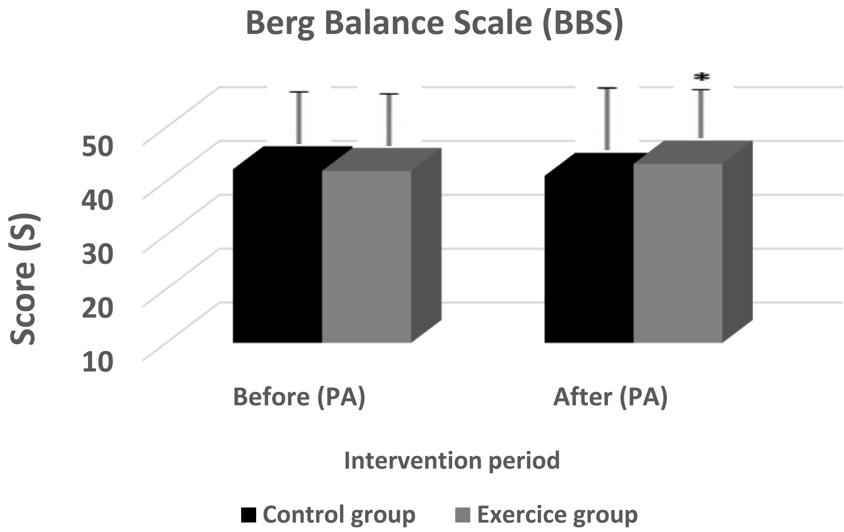

Figure 3. Berg Balance Scale test comparisons within and between groups at baseline and post-intervention. Values are means (±SD). * Significantly different ($p < 0.05$) for the intervention group after 12 weeks of multicomponent physical training program.

A beneficial impact of physical exercise was seen in the intervention group with significant results in the timed up and go test; the time between starting and ending the test was improved, and the interaction group × training was significant ($p = 0.001$), whereby the intervention group improved more than the control group, who performed worse in the test (IG = 14.5%; CG = 7.11%) (Figure 4).

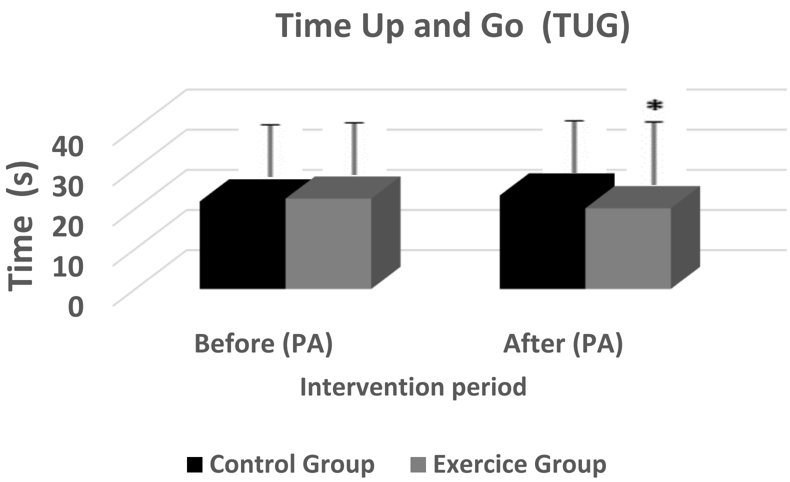

Figure 4. Timed up and go test comparisons within and between groups at baseline and post-intervention. Values are means (±SD). * Significantly different ($p < 0.05$) for the intervention group after 12 weeks of multicomponent physical training program.

After the intervention period, our results show a significant improvement in most of the physical tests, except the WTT (Figure 5); patients had many difficulties in realizing the dual-tasks performance test, and there was no significant effect of group, time or interaction (all, $p > 0.05$).

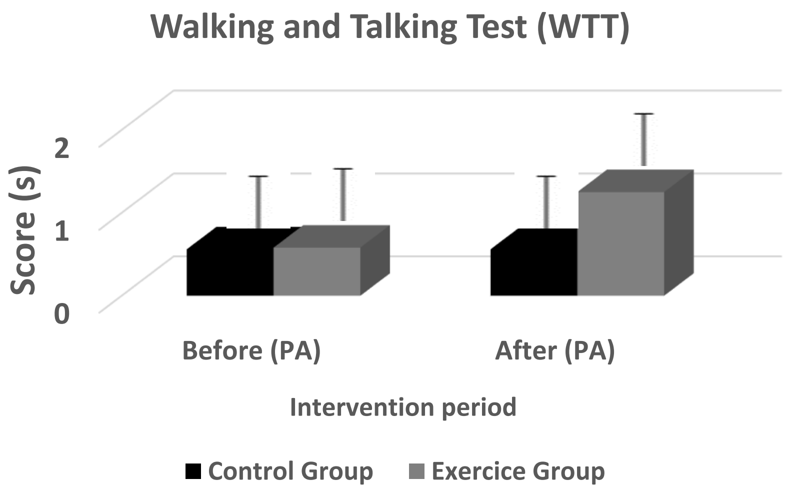

Figure 5. Walking and talking test comparisons within and between groups at baseline and post-intervention. Values are means (±SD).

3.2. Effect of Physical Activity on Biochemical Parameters

At baseline, the intervention group had a greater BMI (p = 0.003) and lower creatinine (p = 0.003) triglycerides (p < 0.001), Ca, (p = 0.011) and K (p = 0.036) than the intervention group. As shown in Tables 1 and 3, there was no effect of training on biochemical parameters (p > 0.05).

Table 3. Baseline biochemical parameters for Alzheimer's patients in a control and intervention group.

Variable	Control Group	Intervention Group	*p*-Value
Red blood cell count ($\times 10^9$/L)	3.86 ± 0.57	4.11 ± 0.28	0.196
White blood cell count ($\times 10^9$/L)	6284.44 ± 545.85	6717.75 ± 552.13	0.090
Hemoglobin (g/dL)	13.52 ± 0.94	13.91 ± 0.61	0.262
Platelet count	279.08 ± 47.79	277.33 ± 28.67	0.918
Hematocrit (%)	43.35 ± 2.68	42.81 ± 2.44	0.635
Triglycerides (mg/dL)	2.14 ± 0.30	42.81 ± 2.44	<0.001
Cholesterol (mg/dL)	4.12 ± 0.60	3.76 ± 0.88	0.310
Total bilirubin (mg/dL)	8.79 ± 0.89	8.76 ± 0.63	0.917
Aspartate transaminase (ASAT)	14.44 ± 1.42	14.50 ± 1.98	0.944
Alanine transaminase (ALAT)	12.00 ± 1.12	12.17 ± 1.47	0.780
Blood pressure (mmHg)	85.44 ± 6.04	84.88 ± 4.96	0.815
Creatinine (mg/dL)	138.44 ± 4.98	117.42 ± 17.73	0.003
Urea (mg/dL)	4.61 ± 0.81	4.90 ± 1.13	0.525
Glucose (mg/dL)	4.01 ± 0.88	3.93 ± 0.78	0.812
Sodium (Na) (mEq/L)	140.78 ± 9.67	142.50 ± 7.79	0.656
Calcium (Ca) (mEq/L)	3.68 ± 1.10	2.66 ± 0.54	0.011 *
Potassium (K) (mEq/L)	4.27 ± 1.03	3.42 ± 0.70	0.036 *

* Significantly different between groups (p < 0.05).

4. Discussion

The objective of this study was to investigate the effects of a three-month multicomponent training program on physical functions and biochemical parameters in older patients with Alzheimer disease. We adopted a simple and comprehensive protocol to identify the effects of PA on motor and biochemical functions. In addition, we objectively assessed various physical tests that can be easily performed with minimal equipment. However, as performance on these tests requires the patients to understand the instructions and be motivated to complete the tests, the results in part fulfilled our expectation; the individuals with Alzheimer disease who participated in the exercise program presented improvement in walking parameters with better mobility and postural capacity, which confirm the importance of this type of non-pharmacological treatment for older patients with Alzheimer disease.

4.1. Intervention

Alzheimer's is generally considered as a disease mainly affecting both cognitive and motor function. Van Doorn et al. [52] drew attention to the fact that Alzheimer patients are twice as likely to fall as healthy aged persons. Physical disorders generally take place while the subject is walking, which is to say over the course of a dynamic activity. The physical program that we applied in this study proved to be a safe intervention in relation to the objectives fixed from the beginning of this study. We considered the beneficial effects of physical exercise on risk factors for falls and fractures, such as cognitive decline, loss, gait and balance, as well as the positive effects on quality of life and autonomy for AD patients, as stated in some previous studies [53]. In addition, we conducted a group intervention to enhance the beneficial effects of collective work, although with a small number of participants [54] to provide individualized attention according to the needs of each patient. Despite the American College of Sports Medicine and some other studies providing evidence of the beneficial impacts of unsupervised physical activity [55], other studies reported a better effect produced by systematized and supervised physical exercise [56].

4.2. Effects of Physical Activity on Functional Parameters

To examine the impact of the intervention on physical functions, balance and gait disturbances were evaluated as risk factors in older patients with Alzheimer's. Some of the most commonly used tests in elderly people and Alzheimer's patients were used for this purpose. However, the variety of parameters around the interventions and assessment tools used in the previous studies complicates comparisons. A scientific and clinical consensus on these aspects is required. As for our study, it shows a positive impact of physical exercises on mobility and balance efficiency in our patients, which may consequently decrease the risk of physical functions, as was shown by Toulotte et al. [57]. Regarding the time up and go test, gait and balance were improved in AD patients following 12 weeks of a multicomponent training program by (14.50%), a more significant test result compared with other studies. De Andrade et al. [58] and Yao et al. [59] reported a decreasing of about two seconds with a four-month intervention, an improvement that we obtained in the first month, which was maintained. We also saw improvement in the Tinetti test (53.40%), Berg Balance Scale (3.17%) and the walking and talking test (115%). As such, exercises should focus on improving gait and dynamic balance during voluntary movements as well as during unpredictable disturbances [60]. To ensure the effectiveness of training, balance and walking should be trained with verbal instructions as a basic element [61]. Gras et al. [62] recruited a sample of 13 mild-AD adults (~73 years old) matched with 13 subjects without AD. Participants with mild AD had significantly shorter times in the sharpened Romberg tests with eyes open and closed compared to the controls.

Results concerning the 6-min walking test show a significant improvement in walking distance concerning the intervention group (52.50%); the finding of this result is in line with other published data [63]. Improvements in functional performances, such as a better walking ability, was observed after the physical program in older patients with Alzheimer disease [64]. Various types of exercise improve walking parameters such as gait speed [65], double support time [66] and stride length [67]. Our exercise program significantly increased the mean score of the Tinetti test in patients of the intervention group; this finding of improvement is in agreement with the study of Santana-Sosa et al. [68], who found that a multicomponent training program improved the score of the Tinetti test and the time up and go tests, two simple and very acceptable tests used to examine the impact of physical activity on physical function [69].

The association among physical activity, walking and balance capacities in older patients has already been examined. According to Rolland et al. [70], significantly heightened walking speed has been observed after 6 months of walking for 12 months with supervision. Leisure time spent engaging in physical activity seems to be particularly protective against AD, even though, given the low-to-moderate quality of studies, current evidence does not permit specific practical recommendations in terms of type, frequency, intensity or duration of PA. Three months of a physical activity program with multiple types of mobility, gait and balance exercises improved physical functions in older patients. As participants already suffer from decreasing muscle mass and strength, balance training has been shown to improve physical capacity and postural ability.

4.3. Effects of Physical Activity on Biochemical Parameters

It is known that physical exercise reduces cardiovascular disorders by increasing the level of high-density lipids (HDL) in the blood [71], reduces low-grade inflammation in coronary artery pathology [72] and may change biochemical biomarkers, but unfortunately, in our results, we did not find an association between physical activity and biochemical parameters. Research on this aspect is still needed to examine if there is a relationship between physical activity and biochemical biomarkers in AD patients [73].

4.4. Limitation

Some limitations of the present study should be noted. First, this study is based on a randomized control study with a small size of patients from both genders. Future studies are needed to determine the benefits of physical activity programs with a larger sample size of elderly patients for both genders. Second, an examination of the effect of physical activity programs on functional parameters with both objective and subjective measures is needed to clarify the positive impact of physical programs on a patient's well-being. Futures studies should quantitatively and qualitatively compare the effects of different types of PE on a patient's life quality. Researchers and health-care workers should pay attention to exercise program adherence in this elderly population.

5. Conclusions

In recent years, numerous studies have indicated many beneficial effects of physical exercise on the physical health of aged patients. However, exercise is increasingly being considered as a standard of care for preventing cognitive and physical disorders. Accordingly, the exercise regimens should be individually tailored to ensure better benefits for all patients [74]. The present study showed that physical exercise programs optimize functional parameters for Alzheimer's patients. The 12 weeks of the multicomponent training program induced positive changes in postural control, walking and mobility functions, especially for the intervention group, who obtained a better result compared with the control group, who had a small improvement. Physical activity can be beneficial in all stages of Alzheimer disease. However, to obtain more insight into the mechanism underlying the impacts of physical activity, we need more high-quality studies. It is of the utmost importance that specific information about the intervention is well-documented, such as the characteristics of the patients and the duration, intensity and different components of the intervention program. This information is important in order to interpret the external validity, possible confounders and the dose–response relationship among physical activity, functional and biochemical parameters.

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Informed Consent Statement: Informed consent was obtained from all subjects and guardians involved in the study.

Data Availability Statement: The data presented in this study are available on reasonable request from R.H.

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