Immune system and quality of life following aerobic exercise versus resistance exercise training among Alzheimer’s

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Abstract

Background: Globally, Alzheimer’s disease (AD) affects millions of elderly individuals are affected with AD who suffer from decline in cognitive ability. However, immune system dysfunction has a role in AD pathogenesis. However, pharmacological therapeutic intervention for caring of ADIs not available. Therefore there is a need to develop novel therapeutic modalities for AD individual care.

Objective: The objective of the this trial was to detect immune system and quality of life (QOL) response following aerobic versus resisted exercise training among AD subjects.

Methods: Fifty older with AD disease the range of age ranged was 61 to 73 years enrolled in the current study. However, smoking, liver, chest, renal, metabolic and cardiac dysfunction considered as exclusion criteria. Participants were randomly enrolled into group (A) who applied aerobic exercise intervention, while group (B) applied resisted exercise intervention for period of six months.

Results: The SF-36 which measure QOL along with in the immunological parameters (CD3 count, CD4 count, CD8 count and CD4/CD8 ratio) showed significant improvement following aerobic and resisted exercise. However, comparing between both groups showed significant differences with greater significant improvement in all measured parameters following aerobic exercise training (p < 0.05).

Conclusion: Aerobic exercise is the most appropriate exercise to improve immune system and quality of life among elderly Alzheimer’s.

Introduction

Alzheimer’s disease (AD) characterized with deteriorated both function, cognition and neuronal loss [1]. Currently, there is about 24 million AD, which expected to reach about 100 million subjects by 2050 around the world [2,3]. The cost of management of the current AD population is greater than 220 billion US dollars, which is expected to reach greater than one trillion by 2050 [4]. Both patient and family are adversely affected by AD as the disease badly deteriorate behavior, cognitive and physical aspects [5].

Evidences proved an association between inflammation of brain tissue and aging changes that drive the pathological changes in AD [6]. The inflammatory changes induces immunological changes promotes AD development [7,8].

Moreover, the majority of AD individuals suffer from many psychiatric disturbances and depression [9-11]. Therefore there is a need to develop novel therapeutic modalities for AD individual care [12].

Evidences reported positive influence of exercise training on immune system [13]. Therefore, it is usually recommended to apply exercise training to positively influence immune system through modulation of systemic inflammatory status and cognitive dysfunction among AD individuals [14-20]. Limited evidences available regarding differences of influence of aerobic and resisted exercises on elderly with AD. The objective of the this trial was to detect immune system and quality of life(QOL) response following aerobic versus resisted exercise training among AD subjects.
Patients and methods

Subjects

Fifty older with AD disease the range of age ranged was 61 to 73 years enrolled in the current study. However, smoking, liver, chest, renal, metabolic and cardiac dysfunction considered as exclusion criteria. Participants were randomly enrolled into group (A) who applied aerobic exercise intervention, while group (B) applied resisted exercise intervention for period of six months. A consent form was signed by legal guardian of all participants before sharing in our study which was ethically approved by FAMS Ethical Research Committee, King Abdulaziz University.

Measurements

A. Flow cytometry analysis: Leukocyte differentiation antigens CD3, CD4 and CD8 were measured using Beckman Coulter, Marseille, France. However, flow cytometry (Cytomics FC 500 and CXP software was used for analysis of samples.

B. Health-related quality of life (SF-36 HRQL): Assessment of quality of life (QOL) was detected using the standard reliable test SF-36 that includes eight subscales: Vitality, Bodily Pain, General Health, Physical Functioning, Social Functioning, Physical Role Functioning, Emotional Role Functioning, and Mental Health [21].

Procedures

1- Group (A): Twenty-five AD elderly subjects received treadmill aerobic exercise training for six months, the training program started with five minutes warming up, thirty minutes of training on the treadmill with an intensity 60% - 80% of individual maximal heart rate and end with five minutes cooling down [22].

2- Group (B): Twenty-five AD elderly subjects received resisted exercise training for six months, the training program started with ten minutes of mobility exercises followed by resisted exercise training on 9 machines of resistance training in order to do resisted training for the main skeletal muscles of the lower limbs, upper limbs and trunk muscles. Training session included 3 sets each set which consisted of 8-12 repetitions with a moment rest in between each 2 set. Training intensity was 60% - 80% of one maximum repetition (1-RM) [23].

Results

Baseline variables of all participants proved that both groups were homogeneous as comparing the both groups regarding baseline and demographic parameters revealed no significant differences (Table 1).

The main findings in the current study showed significant increase in the mean values of SF-36 which measure QOL along with significant improvement in the immunological parameters (CD3 count, CD4 count, CD8 count and CD4/CD8 ratio) following aerobic and resisted exercise training (Tables 2-5). However, comparing between both groups showed significant differences with greater significant improvement in all measured parameters following aerobic exercise training (Tables 6,7).

Discussion

Globally, millions of elderly individuals are affected with AD who suffer from decline in cognitive ability. However, immune system dysfunction play a principal role in AD pathogenesis [24,25]. Recently, there is no available pharmacological therapeutic intervention for caring of AD. However, exercise training is of positive effects on physical and cognitive function of AD individuals [26,27].

Results of current study proved that after six months, immunological parameters (CD3, CD4 and CD8) significantly increased and CD4/CD8 ratio significantly decreased in group (A) applied aerobic exercises greater than group (B) applied resisted exercises. Cell numbers are expected to decrease due to aging process. This finding is consistent with other studies, while other contradicting studies have made different observations. As our results agreed with many researches proved that aerobic exercise training improved immune system of elderly subjects [28-31]. However, Peeri and colleagues, stated that number of CD4 & CD8 cells and physical fitness significantly increased following aerobic exercise for six months in healthy elderly males [32]. While, Kapasi, et al. reported that two months of combined aerobic and resisted exercises improved CD8+ cells among elderly individuals [33]. On the other hand, limited evidences that measure influence of immunological response to resisted exercise are available, the majority of these studies reported that 2-3 months of resisted exercise programs had minimal influence of immune system and inflammatory cytokines [34-38]. While, many studies did not show significant immune function improvement following progressive resistance training [39-43].

Concerning QOL, aerobic exercise associated with greater significant increase in the SF-36 subscale mean values than resisted exercise. Many previous studies approved these findings that indicate that subjects psychological wellbeing and QOL associated with physical exercises [44-47]. Mahendra reported that aerobic exercise training for 3 months improved SF-36 score of in patients with Alzheimer’s disease [48]. However, Bowen et al. proved that postmenopausal women experienced improved QOL following twelve months of exercise intervention [49].In addition, Sørensen, et al. mentioned that 12-month exercise trial improved HRQOL of elderly individuals [50]. Similarly, Imayama, et al. stated that twelve months of moderate to vigorous strength training improved HRQOL improved among overweight men following [51]. In addition, there are evidences reported that exercise training with higher intensity improved mental...
### Table 1: Participants baseline and demographic criteria.

| Characteristic          | Group (A)     | Group (B)     | Significance |
|-------------------------|---------------|---------------|--------------|
| Age (years)             | 63.71 ± 3.95  | 64.24 ± 3.67  | \( p > 0.05 \) |
| Gender (male/female)    | 13/12         | 11/14         | \( p > 0.05 \) |
| Weight (kg)             | 66.13 ± 5.94  | 64.73 ± 4.96  | \( p > 0.05 \) |
| Height (m)              | 1.71 ± 0.08   | 1.66 ± 0.07   | \( p > 0.05 \) |
| BMI (kg/m²)             | 22.76 ± 3.15  | 23.48 ± 3.26  | \( p > 0.05 \) |
| SBP (mmHg)              | 135.92 ± 11.34| 139.27 ± 10.72| \( p > 0.05 \) |
| DBP (mmHg)              | 82.15 ± 8.43  | 84.18 ± 7.24  | \( p > 0.05 \) |
| Glucose (mmol/L)        | 5.12 ± 0.63   | 5.26 ± 0.71   | \( p > 0.05 \) |
| ALT (U/L)               | 38.67 ± 6.22  | 40.28 ± 5.65  | \( p > 0.05 \) |
| AST (U/L)               | 26.53 ± 3.85  | 27.74 ± 3.92  | \( p > 0.05 \) |
| HR\(_{max}\) (beat/min) | 153.23 ± 9.67 | 150.72 ± 8.95 | \( p > 0.05 \) |

BMI: Body Mass Index; SBP: Systolic Blood Pressure; DBP: Diastolic Blood Pressure; AST: Aspartate Aminotransferase; SBP: Systolic Blood Pressure; HR\(_{max}\): Maximum Heart Rate.

### Table 2: Statistical analysis of the immunological parameters before and at the end of the study of group (A).

| SF-36 subscale variables | Mean ± SD | t - value | Significance |
|--------------------------|-----------|-----------|--------------|
| CD3 count (10⁹/L)        | 1.95 ± 0.83| 1.24 ± 0.66* | 5.37 | \( p < 0.05 \) |
| CD4 count (10⁹/L)        | 1.73 ± 0.94| 1.12 ± 0.72* | 5.64 | \( p < 0.05 \) |
| CD8 count (10⁹/L)        | 0.97 ± 0.32| 0.51 ± 0.24* | 4.83 | \( p < 0.05 \) |
| CD4/CD8 ratio            | 1.69 ± 0.81| 1.14 ± 0.69* | 5.16 | \( p < 0.05 \) |

(*) indicates a significant difference between the two groups, \( p < 0.05 \).

### Table 3: Statistical analysis of SF-36 subscale scores before and at the end of the study of group (A).

| SF-36 subscale variables | Mean ± SD | t - value | Significance |
|--------------------------|-----------|-----------|--------------|
| SF-36: Health transition | 2.73 ± 0.94| 1.53 ± 0.65* | 4.31 | \( p < 0.05 \) |
| SF-36: Physical functioning| 71.76 ± 7.23| 82.11 ± 7.83* | 6.19 | \( p < 0.05 \) |
| SF-36: Role functioning: Physical | 77.54 ± 8.36| 89.32 ± 9.27* | 7.13 | \( p < 0.05 \) |
| SF-36: Bodily pain       | 76.81 ± 8.19| 67.58 ± 7.63* | 6.97 | \( p < 0.05 \) |
| SF-36: General health    | 70.65 ± 7.23| 81.87 ± 7.42* | 7.26 | \( p < 0.05 \) |
| SF-36: Vitality          | 58.22 ± 5.15| 68.75 ± 5.91* | 5.23 | \( p < 0.05 \) |
| SF-36: Social functioning| 84.37 ± 7.13| 93.41 ± 7.85* | 8.78 | \( p < 0.05 \) |
| SF-36: Role functioning: Emotional | 91.25 ± 9.84| 82.16 ± 9.57* | 8.27 | \( p < 0.05 \) |
| SF-36: Mental health     | 83.62 ± 7.27| 71.45 ± 6.42* | 8.11 | \( p < 0.05 \) |

(*) indicates a significant difference between the two groups; \( p < 0.05 \).

### Table 4: Statistical analysis of the immunological parameters before and at the end of the study of group (B).

| SF-36 subscale variables | Mean ± SD | t - value | Significance |
|--------------------------|-----------|-----------|--------------|
| CD3 count (10⁹/L)        | 1.97 ± 0.76| 1.62 ± 0.73* | 3.21 | \( p > 0.05 \) |
| CD4 count (10⁹/L)        | 1.79 ± 0.84| 1.37 ± 0.82* | 2.98 | \( p > 0.05 \) |
| CD8 count (10⁹/L)        | 0.98 ± 0.30| 0.76 ± 0.33* | 2.75 | \( p > 0.05 \) |
| CD4/CD8 ratio            | 1.72 ± 0.79| 1.51 ± 0.76* | 2.83 | \( p > 0.05 \) |

### Table 5: Statistical analysis of SF-36 subscale scores before and at the end of the study of group (B).

| SF-36 subscale variables | Mean ± SD | t - value | Significance |
|--------------------------|-----------|-----------|--------------|
| SF-36: Health transition | 2.87 ± 0.81*| 2.21 ± 0.73 | 2.57 | \( p < 0.05 \) |
| SF-36: Physical functioning| 68.95 ± 6.74*| 75.32 ± 7.25 | 3.21 | \( p < 0.05 \) |
| SF-36: Role functioning: Physical | 75.32 ± 7.6*| 82.13 ± 8.36 | 3.12 | \( p < 0.05 \) |
| SF-36: Bodily pain       | 78.15 ± 8.23*| 73.28 ± 7.64 | 3.25 | \( p < 0.05 \) |
| SF-36: General health    | 69.72 ± 7.21*| 74.19 ± 6.32 | 3.16 | \( p < 0.05 \) |
| SF-36: Vitality          | 56.87 ± 5.92*| 61.42 ± 6.11 | 3.34 | \( p < 0.05 \) |
| SF-36: Social functioning| 83.95 ± 8.36*| 88.75 ± 9.13 | 3.29 | \( p < 0.05 \) |
| SF-36: Role functioning: Emotional | 91.78 ± 9.81*| 86.14 ± 9.52 | 3.13 | \( p < 0.05 \) |
| SF-36: Mental health     | 83.86 ± 7.23*| 78.23 ± 6.91 | 3.37 | \( p < 0.05 \) |

(*) indicates a significant difference between the two groups; \( p < 0.05 \).

### Table 6: Statistical analysis of the immunological parameters at the end of the study of group (A) and group (B).

| SF-36 subscale variables | Mean ± SD | t - value | Significance |
|--------------------------|-----------|-----------|--------------|
| CD3 count (10⁹/L)        | 1.24 ± 0.66*| 1.62 ± 0.73 | 2.98 | \( p < 0.05 \) |
| CD4 count (10⁹/L)        | 1.12 ± 0.72*| 1.37 ± 0.82 | 2.87 | \( p < 0.05 \) |
| CD8 count (10⁹/L)        | 0.51 ± 0.24*| 0.76 ± 0.33 | 2.62 | \( p < 0.05 \) |
| CD4/CD8 ratio            | 1.14 ± 0.69*| 1.51 ± 0.76 | 2.74 | \( p < 0.05 \) |

(*) indicates a significant difference between the two groups, \( p < 0.05 \).
health greater than lower intensity exercise training [52,53]. While, Hoffmann, et al. found that AD subjects gained great improvement in QOL and physical fitness following aerobic of moderate intensity [54]. The specific mechanism for improved QOL following exercise training is not well known. However, improved self-perceptions, self-efficacy, activity of neurotransmitters [55-57], neuronal survival [58], synaptic plasticity [61], brain plasticity and vascularization [62-64], along with reduced emotional strain associated with social contact [65].

**Conclusion**

Aerobic exercise is more appropriately improve quality of life and immune system among elderly Alzheimer’s.

**Acknowledgment**

Author wants to express her thanks for staff members of Physical Therapy Department, Faculty of Applied Medical Sciences, King Abdulaziz University for their support in application of therapeutic intervention in this manuscript.

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