Effectiveness of Exercise on Reducing Fatigue in Parkinson’s Disease: A Systematic Review

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Received: October 25, 2017; Published: November 25, 2017

Abstract

Purpose: Parkinson’s disease (PD) is characterized by motor and nonmotor symptoms, such as bradykinesia, rigidity, fatigue, and cognitive impairments etc. Fatigue is one of the most debilitating symptoms, and voted as the leading symptom in need of research by patients with PD. However, there is a lack of effective treatment for PD-fatigue. Limited evidence suggests that exercise training improves fatigue in PD. The purpose of this systematic review was to evaluate the effectiveness of exercise program on reducing fatigue in patients with PD.

Methods: A systematic search of databases CINAHL Complete, PubMed, and PEDro (Physiotherapy Evidence Database) was performed using terms: “Parkinson’s disease” AND (“exercise” OR “physical therapy” OR “physical activity”) AND “fatigue”. To be included in this review, the studies had to be randomized controlled trials, and to meet the following criteria: 1) examining patients with PD; 2) using exercise training such as aerobic exercise, treadmill training, or exergaming etc.; 3) having fatigue as an outcome measure; and 4) at least 4 out of 10 on the PEDro scale.

Results and Discussion: Seven randomized controlled trials published between 2012 and 2017 were included in this review. Six of the seven studies demonstrated statistically significant reductions in fatigue following exercise programs. This review showed that multiple modes of exercise interventions were effective in reducing PD-related fatigue.

Conclusions: Exercise program may be effectively utilized as an integral component of clinical management of PD-related fatigue and other symptoms, ultimately maximizing the quality of life in patients with PD.

Keywords: Parkinson’s Disease; Fatigue; Exercise; Physical Therapy; Effectiveness

Abbreviations

FSS: Fatigue Severity Scale; LSVT: Lee Silverman Voice Training; MFIS: Modified Fatigue Impact Scale; MS: Multiple Sclerosis; PD: Parkinson’s Disease; PEDro: Physiotherapy Evidence Database; RCT: Randomized Controlled Trial

Introduction

Parkinson’s disease (PD) is a progressive neurodegenerative disease due to a loss of dopamine-producing neurons in the basal ganglia [1,2]. PD is clinically characterized by both motor and nonmotor symptoms: including bradykinesia, rigidity, tremor, and anxiety, fatigue, sleep disorders, health-related quality of life etc [3,4]. Individuals with PD frequently report that fatigue is one of the most debilitating symptoms associated with PD. And fatigue has been voted the number one symptom in need of research by patients with PD [5,6]. Although fatigue has a significantly negative impact on quality of life in patients with PD, there is a lack of effective treatment for PD-related fatigue as anti-PD medication shows equivocal results in combating this non-motor symptom [7-9].
Fatigue is a common symptom of a variety of neurological disorders such as multiple sclerosis (MS), stroke, and poliomyelitis [10]. Exercise interventions have been shown to be effective in combating fatigue associated with progressive neurological disorders. A 20-week stepwise physical activity program focused on gradual stretching, resistance, and aerobic exercise for patients with MS demonstrated significant decreases in measures of fatigue severity [11]. Dalgas., et al. [12] examined the effect of exercise on MS-associated fatigue by randomly assigning 54 patients with MS to 15-week aerobic training or a non-exercise condition. The results demonstrated that the group receiving exercise had a significant reduction in fatigue.

Limited evidence suggests that exercise can potentially reduce PD-related fatigue [13]. The objective of this systematic review study was to evaluate the effectiveness of specific type of exercise therapy compared with conventional care on management of fatigue in patients with Parkinson’s disease.

Materials and Methods

This systematic review followed the PRISMA (preferred reporting items for systematic reviews and meta-analyses) criteria [14].

Inclusion and Exclusion Criteria

Types of the Study

To be included in this review, a study had to be conducted using a randomized controlled trial (RCT), and had a score of at least 4 out of 10 on the scale of Physiotherapy Evidence Database (PEDro scale) [15].

Types of Participants

Only studies examining participants diagnosed with idiopathic PD were included in this review. In addition, the studies with participants treated by deep brain stimulation were excluded.

Types of Interventions

This review included RCTs that examined exercise intervention, such as treadmill walking, aerobic training, Lee Silverman Voice Training (LSVT BIG therapy), and Argentine tango therapy. Clinical trials assessing effects of dopaminergic medication on fatigue were excluded from this review.

Types of Outcome Measures

The study was included if outcome measures included fatigue. Measurement tools were Modified Fatigue Impact Scale (MFIS), Parkinson Fatigue Scale (PFS), and Fatigue Severity Scale (FSS) all of which sustain measures of fatigue [16-18].

Search strategies

A systematic search of CINAHL Complete, PubMed, and PEDro was administered to obtain published studies until October 2017. A manual search was also performed by checking the references of the eligible studies. Specific search terms and keywords with the subject heading were utilized. The following keywords were used in the search:

- “Parkinson’s Disease” OR “Parkinson”
  AND
- “Physical Therapy” OR Exercise OR "Physical Activity”
  AND
- “Fatigue”

Data Collection and Analysis

Selection of Studies/Screening

Two reviewers (SM and MH) independently screened the articles based on the titles and abstracts to determine whether they met the inclusion criteria. After screening the abstract and titles, two reviewers completed a full text analyses of the articles to determine if each
study met the inclusion and exclusion criteria, followed by a third reviewer (RX) to review all full text articles for verification. Relevant data were extracted from articles that met the inclusion criteria. Table 1 lists the study design, sample size, interventions, outcomes, and PEDro scores of the seven included studies.

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year</th>
<th>Study Design</th>
<th>Participants (N)</th>
<th>Intervention (Experimental)</th>
<th>Comparative Intervention</th>
<th>Outcome Measures</th>
<th>PEDro scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Canning., et al.</td>
<td>2012</td>
<td>RCT*</td>
<td>N = 20</td>
<td>Semi-supervised home based Treadmill Walking</td>
<td>Usual Care- advice to maintain current level of physical activity</td>
<td>Modified Fatigue Impact Scale (MFIS)</td>
<td>8/10</td>
</tr>
<tr>
<td>Cugusi., et al.</td>
<td>2015</td>
<td>RCT</td>
<td>N = 20</td>
<td>12-week Nordic Walking program</td>
<td>Conventional care</td>
<td>Parkinson’s Fatigue Scale</td>
<td>4/10</td>
</tr>
<tr>
<td>Dashtipour., et al.</td>
<td>2014</td>
<td>RCT</td>
<td>N = 11</td>
<td>Lee Silverman Voice Training (LSVT) BIG Therapy</td>
<td>General Exercise</td>
<td>MFIS</td>
<td>5/10</td>
</tr>
<tr>
<td>Ribas., et al.</td>
<td>2017</td>
<td>RCT</td>
<td>N = 20</td>
<td>Exergaming</td>
<td>Conventional Exercise</td>
<td>Fatigue Severity Scale (FSS)</td>
<td>7/10</td>
</tr>
<tr>
<td>Romenets., et al.</td>
<td>2014</td>
<td>RCT</td>
<td>N =33</td>
<td>Argentine tango partnered classes</td>
<td>Self-directed exercise group</td>
<td>FSS</td>
<td>6/10</td>
</tr>
<tr>
<td>Uc., et al.</td>
<td>2015</td>
<td>RCT</td>
<td>N = 60</td>
<td>Continuous Training of aerobic walking</td>
<td>Interval Training of aerobic walking</td>
<td>FSS</td>
<td>5/10</td>
</tr>
<tr>
<td>Winward., et al.</td>
<td>2012</td>
<td>RCT</td>
<td>N =39</td>
<td>12-week Community Exercise Program</td>
<td>Conventional care</td>
<td>FSS</td>
<td>8/10</td>
</tr>
</tbody>
</table>

Table 1: Characteristics of the included study.

* RCT: Randomized Controlled Trial

Assessment of Methodologic Rigor

All included articles were assessed using PEDro scale which is a tool for evaluating and quantifying methodologic quality of clinical trials. The PEDro scale is utilized to assist the reviewers in determining the construct validity and internal validity of included studies, and inclusion of statistically significant data to make results interpretable of each study. In addition, external validity was also assessed (Criterion 1), but this criterion is not included in final count of the PEDro score [15].

Results and Discussion

Study Selection

The initial search of databases and other sources resulted in a total of 916 articles with 63 articles remaining after a thorough screening of titles and abstracts. The 56 articles were determined to be ineligible, as they did not include exercise program but pharmacologic regimen, did not measure fatigue as an outcome, nor utilized an RCT design. Ultimately, seven articles met the inclusion and exclusion criteria, and were thus included in this review [19-25]. Figure 1 is a flowchart illustrating the selection process of the articles for this study.

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Study Characteristics

The included studies were published between 2012 and 2017, and were randomized control trials with the control group also receiving treatment. Of the seven studies, six reported improvements in fatigue after the exercise interventions.

Most of the interventions included some type of aerobic exercise, resistance, balance, and home-based treadmill walking program. A few studies focused on more specific aspects of exercise, including a Nordic Walking program [20], Exergaming [22], Argentine tango therapy [23], and LSVT BIG therapy [21].

Outcomes

Canning., et al. [19] showed significant improvement in fatigue in the group receiving home-based treadmill training (p < 0.05). Nordic Walking was found to significantly (p < 0.05) reduce fatigue [20]. Dashtipour, et al. [21] reported statistically significant improvements in

Figure 1: PRISMA flowchart: Study Selection Process.
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the MFIS score at 6-month posttests for both LSVT BIG and General Exercise groups (p < 0.05). Uc., et al. [24] reported a significant improvement in the Fatigue Severity Scale upon continuous training of aerobic walking (p < 0.01). Ribas., et al. [22] found that Exergaming had significantly improved fatigue (p < 0.05). Modest borderline improvements in the FSS (p < 0.057) were demonstrated by participation in 1 hour sessions of traditional Argentine tango twice weekly for 12 weeks [23]. On the other hand, Winward., et al. [25] found no significant changes in fatigue between the two groups in response to a community gym-based exercise program and conventional care (p = 0.76) or from baseline to 3-month posttest.

This systematic review aimed to examine the effectiveness of exercise and physical activity on treatment of fatigue in PD. Physical activity and its effect on PD-fatigue is an understudied topic of research. Of the 7 articles that met the review criteria, six demonstrated significant improvements in fatigue levels.

Fatigue has long been recognized in other neurological conditions including MS, stroke, and poliomyelitis [10]. Effects of exercise therapy has relatively been well studied and proven to be effective in managing fatigue associated with MS [26-28]. Aerobic exercise has been most studied regarding its effects on the neuronal connections and on reducing fatigue in MS. Progressive resistance training targeted toward lower limb musculature in patients with MS has been found to decrease levels of fatigue by increasing muscular endurance [26]. Heine., et al. [27] shows that endurance exercise training has a neuroprotective effect, and can induce physiological and psychological changes that counteract the impact of fatigue in patients with MS. Considering that exercise has been demonstrated to reduce fatigue in other neurodegenerative disease, it is plausible to expect that exercise therapy plays a role in reducing fatigue in patients with PD.

In addition, Pavese., et al. reported an association of fatigue in PD with altered transmission of serotonin through the striatal and limbic pathways [29]. Both groups of subjects with PD (one group with fatigue and the other without fatigue) underwent imaging protocols using 18F-dopa and 11C-DASB, biomarkers of dopamine storage capacity and serotonin transporter availability. None had experienced depression or sleep disturbance. Results showed that subjects with PD-fatigue had significantly lower serotonin transporter binding than did subjects without fatigue. Authors concluded that PD-fatigue is associated with reduced serotonergic function in the basal ganglia and limbic structures as well as potentially with insular dopaminergic dysfunction. The findings implied that strategies to increase brain level of serotonin would be a rational approach for relieving fatigue symptom in Parkinson’s disease [29]. Exercise program has been demonstrated to increase serotonin synthesis and function of the brain in mental disorders such as depression as well as several rodent studies [30]. Prescription of an exercise program in patients with PD-fatigue has the potential to enhance serotonin transmission within the involving areas of the brain, and can therefore decrease fatigue.

Overall, exercise has been shown to have a neuroprotective effect and enhance neuroplasticity [31]. The included studies in this review investigated various types of exercises in regards to the treatment of non-motor symptoms of PD including fatigue. Six of the seven studies showed positive effects of exercise on PD-fatigue, except for the study by Winward., et al. showing that a 12-week gym-based workout that incorporated treadmill training and was largely self-determined, did not result in significant changes in fatigue. Participants’ attendance was attributed to be one of the reasons [25]. In particular, research has also demonstrated five interactions of exercise and neuroplasticity: 1) intensity level directly affects plasticity, 2) the greater the complexity of the action, the greater the adaptation, 3) rewarding activities increase greater dopamine levels and enhance learning, 4) dopaminergic neuron activity and the amount of exercise are closely related, and 5) exercise as treatment in early stage of PD can slow the disease progression [32].

Limitations of the Review

The research articles reviewed in this study had limited sample sizes and primarily focused on motor symptoms of PD. The sample sizes in these research articles ranged from 11 to 60, given that research on efficacy of exercise in management of PD-related fatigue is still merging. The studies included in this review varied in the type of intervention, duration of treatment, and different measures of fatigue: MFIS, FSS, and PFS, due to an understudied topic. No meta-analysis was performed in this systematic review since intervention varied among included studies, and no original data were available. It is also acknowledged that publication bias may exist as only articles in English were included in this review.

Citation: RuiPing Xia., et al. ”Effectiveness of Exercise on Reducing Fatigue in Parkinson’s Disease: A Systematic Review”. EC Neurology 9.1 (2017): 12-19.
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Conclusion
This systematic review suggests that exercise program may be an integral part of treatment of PD-related fatigue and a tailored exercise program may be more effective in reducing fatigue in patients with PD compared to conventional therapy. More evidence is needed to elucidate the efficacy of exercise intervention and to guide clinical practice in management of fatigue and other debilitating symptoms in PD.

Acknowledgements
None.

Conflict of Interest
Authors of this study have no financial interest or conflict of interest.

Bibliography

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