

Exercise and Restless Legs Syndrome: A Randomized Controlled Trial

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Background and Objectives: Restless legs syndrome (RLS) is a common, underdiagnosed neurological movement disorder of undetermined etiology. The primary treatments for restless legs syndrome are pharmacological. To date, no randomized controlled trials have examined the effectiveness of an exercise program on the symptoms of RLS.

Methods: Study participants (N = 41) were randomized to either exercise or control groups. 28 participants (average age 53.7; 39% males) were available and willing to begin the 12-week trial. The exercise group was prescribed a conditioning program of aerobic and lower-body resistance training 3 days per week. Restless legs symptoms were assessed by the International RLS Study Group (IRLSSG) severity scale and an ordinal scale of RLS severity at the beginning of the trial, and at 3, 6, 9, and 12 weeks.

Results: Twenty-three participants completed the trial. At the end of the 12 weeks, the exercise group (N = 11) had a significant improvement in symptoms compared with the control group (N = 12) ($P = .001$ for the IRLSSG severity scale and $P < .001$ for the ordinal scale).

Conclusions: The prescribed exercise program was effective in improving the symptoms of RLS. (J Am Board Fam Med 2006;19:487-93.)

Background and Objectives

Restless Legs Syndrome (RLS) is a common neurological movement disorder affecting a large segment of the population. Studies of the prevalence of RLS suggest the condition affects approximately 10% of the adult population, although one study found a prevalence of 24% in patients presenting to a primary care office.¹⁻³ Although RLS is common, it is seldom diagnosed. The 2001 Sleep in America Poll found a prevalence of 13% in the adult population, but only 3% of those had actually been diagnosed with RLS.⁴ Factors associated with higher incidence of RLS include older age, multiparity, sedentary lifestyle, positive family history, and obesity.^{1,2} Secondary causes of RLS include

iron deficiency, renal failure, neuropathy, pregnancy, and certain medications.⁵ RLS is associated with depression, anxiety, and negative quality of life.^{6,7}

The diagnosis of RLS is clinical. Minimal criteria for the diagnosis are: 1) a compelling urge to move the limbs, usually associated with paresthesias/dysesthesias; 2) motor restlessness as seen in activities such as floor pacing, tossing and turning in bed, and rubbing the legs; 3) symptoms worse or exclusively present at rest (ie, lying, sitting) with variable and temporary relief by activity; and 4) symptoms worse in the evening and at night.⁸

RLS tends to cluster in older, overweight adults,^{6,9,10} who are at increased risk for comorbid conditions. Physical activity and exercise may be important in the reduction of the risk for comorbid conditions; however, the effects of exercise on RLS severity are unknown. Furthermore, the current treatment for RLS is primarily pharmacological in nature. The vast majority of clinical trials have concentrated on the use of dopaminergic agents, anticonvulsants, and benzodiazepines.¹¹⁻¹³ These agents often have significant side effects. Little research has been undertaken to determine whether lifestyle changes, such as exercise interventions, can improve the symptoms of RLS.

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RLS symptoms typically occur during periods of inactivity and are generally alleviated, at least temporarily, by movement⁵; however, the association between physical activity and RLS symptoms is unclear. Individuals with RLS frequently abstain from vigorous exercise because it has been reported anecdotally that such participation can exacerbate symptoms. Furthermore, current clinical guidelines make no mention of exercise or physical activity recommendations⁵; however, popular patient-oriented Web sites, such as (www.wemove.org) advocate light to moderate exercise over vigorous exercise, even though there is no compelling research to support this recommendation.

Epidemiologic studies have shown a link between RLS and physical activity.^{1,14} Ohayon and colleagues reported physical activity performed close to bedtime was associated with a significantly increased risk of RLS¹⁴; however, a separate study reported a significant link between lack of exercise and risk of RLS.¹ Therefore, the association between RLS and physical activity remains unclear. Possible reasons for the conflicting findings may be: differing diagnostic criteria for RLS, disparate operational definitions of physical activity and exercise, and reliance on measures of physical activity that have not been validated.

In a literature search, no clinical trials evaluating the efficacy of exercise in the treatment of RLS in the general population were identified (Medline search in September 2005 with keywords “restless legs syndrome AND exercise”; “restless legs syndrome AND physical activity”; “restless legs syndrome AND RCT”). However, exercise has been shown to improve symptoms of RLS and periodic limb movements in individuals with spinal cord injuries.^{15,16}

A need exists for randomized controlled trials that study the effectiveness of non-pharmacological interventions for the treatment of RLS. A treatment such as exercise would be useful in taking a multidimensional approach to management that is currently used with most chronic diseases. This study was designed to evaluate the effects of a conditioning program on the symptoms of RLS. The primary hypothesis was that a conditioning program, consisting of an aerobic component and a lower extremity resistance component, would improve the symptoms of RLS.

Methods

Overview of Study Design

The study was a randomized controlled trial of an exercise program for adults with RLS. The exercise program consisted of 12 weeks of aerobic and resistance exercise performed at a hospital-based wellness center. Outcome measures were assessed at baseline as well as 3, 6, 9, and 12 weeks.

Participants and Recruitment

Participant recruitment was accomplished via television advertisements, notices in local newspapers, and flyers placed in patient areas of an academic medicine primary care clinic. To maximize recruitment, potential participants were prescreened over the telephone before visiting the study site for formal testing. Prescreening eligibility relied on answering yes to the following questions, which are based on the diagnostic criteria for RLS⁸:

1. Do you have the desire to move the legs in association with unusual or uncomfortable sensations within the legs?
2. Do you feel the need to move your legs in response to these sensations?
3. Do these sensations become obvious or worse while at rest (during periods of inactivity or relaxation) and may be temporarily diminished by voluntary movements of the legs?
4. Do these sensations occur most frequently during the evening or the early part of the night?

Additionally, participants had to be willing to travel to the study site, accept randomization into either an exercise or control group, and confirm that they were not involved in another ongoing research project. Eligible participants from telephone prescreening were brought to the study site for further evaluation by a physician to confirm the diagnosis of RLS, rule out secondary causes, and assure the absence of exclusion criteria.

Participants were excluded from this study for the following reasons: orthopedic condition that limited ambulation on a treadmill or ability to perform prescribed resistance exercises, recent coronary event in the preceding six months, uncontrolled hypertension, renal dysfunction (serum creatinine greater than 1.5 mg/dL) or anemia (hemoglobin <13 g/dL in males and <11 g/dL in females). Information for these exclusion criteria

were obtained from the potential participants on-site by the examining physician during the screening physical, which included laboratory analysis of hemoglobin and creatinine. The study physician was then responsible for determining participant suitability for the study. This study was approved by the local institutional review board, and informed consent was obtained in a manner consistent with federal guidelines.

Procedures

Following baseline data collection, qualified participants were placed in a pool and were randomized in waves of 10 using a computer-generated list of random numbers. Participants were randomized, in equal numbers, to either the control group or the exercise group. Both groups were instructed in lifestyle interventions that are thought to improve RLS, including cigarette and alcohol cessation, avoidance of excessive caffeine, and proper sleep hygiene. Both groups returned to the study site at 6 and 12 weeks, at which time they completed assessment tools and were asked about changes in medications or health status. Additionally, participants in both groups were contacted via telephone at 3 and 9 weeks to assess RLS symptom severity.

Measures

Restless leg severity was assessed using the International RLS Study Group (IRLSSG) Scale. This validated 10-item questionnaire was designed to assess symptom severity, frequency, and impact on daily life.¹⁷ Participants completed this questionnaire (assistance was available when needed) at baseline, 6, and 12 weeks, and study personnel blinded to allocation called participants at 3 and 9 weeks to complete the questionnaire over the phone. RLS symptom severity score was determined by summing the questionnaire answers. The maximum score is 40, and a higher score indicates more severe RLS. The total score on the RLS Rating Scale questionnaire was used as the primary outcome measure of RLS severity. Participants also rated overall RLS severity on a scale of 1 to 8, with 1 representing mild symptoms and 8 representing severe symptoms.

Participant physical activity levels were assessed using the CHAMPS physical activity questionnaire for older adults.¹⁸ This questionnaire has been shown to be reliable and valid in the older adult population.¹⁹ The CHAMPS is formatted to assess

physical activity in a typical week over the last 4 weeks.

Exercise Intervention Design

The exercise intervention consisted of lower body resistance exercises performed 3 times a week for 12 weeks and treadmill walking for aerobic exercise. The intervention was conducted at a local hospital-based community wellness center with standard exercise equipment and facilities. Following randomization into the exercise intervention group, participants underwent exercise program orientation, which was conducted individually with a certified exercise physiologist. At this visit, participants were first instructed in the use of the treadmill, which included heart rate assessment capability. Walking intensity and duration prescriptions were made in accordance with recommendations of the American College of Sports Medicine current at the time of the study.²⁰ Participants were instructed to walk for 30 minutes, including a 5 minute warm-up and cool-down, at 40% to 60% of their age-predicted maximum heart rate. Participants were also instructed in the use of the Borg rating of perceived exertion (RPE) scale,²¹ and were instructed to maintain exercise intensity that elicited an RPE of 10 to 13.²⁰

During this orientation, muscular strength was assessed using a standardized 10-repetition maximum approach, from which one repetition maximum (1-RM) was estimated. The exercise prescription for strength training was made at approximately 50% of the estimated 1-RM. Most of the study participants had never engaged in resistance training; therefore, a low intensity starting point was established for 3 reasons: 1) to familiarize participants with the proper lifting technique, 2) to reduce risk of discomfort and injury, and 3) increase participant adherence to the exercise intervention. Participants were instructed to perform one set of 8 to 12 repetitions of each exercise for the first 2 weeks to provide an introductory period. Following this 2-week period, participants were asked to increase their training to 2 sets of 8 to 12 repetitions of each exercise for the remainder of the exercise intervention. Exercise progression was achieved by instructing participants to increase the weight lifted in a specific exercise when they could perform 2 sets of 12 repetitions without maximal exertion on 2 consecutive training days. The strength training activities included horizontal leg press, leg exten-

Table 1. Baseline Characteristics of Participants with RLS by Treatment Group (N = 28)

| Background Characteristics | Exercise Group (N = 11) | Control Group (N = 17) | <i>t</i> Test Value | <i>P</i> Value |
|----------------------------|----------------------------|---------------------------|---------------------|----------------|
| Age (years) | | | | |
| Mean | 53.3 | 53.9 | | |
| SD | 9.9 | 9.9 | 0.17 | .863 |
| Gender | | | | |
| Male | 7 (64%) | 4 (24%) | 5.87 | .053 |
| Female | 4 (37%) | 13 (76%) | | |
| Race | | | | |
| Caucasian | 11 (100%) | 16 (94%) | 0.79 | .673 |
| Height (inches) | | | | |
| Mean | 69.1 | 65.7 | | |
| SD | 3.5 | 3.7 | -2.31 | .030 |
| Weight (pounds) | | | | |
| Mean | 205.1 | 176.6 | | |
| SD | 50.4 | 48.4 | -1.48 | .151 |

sion, leg curl, hip adduction, hip abduction, and seated rotary calf press.

The exercise program was completed on an individual basis (eg, not group format), and the participants were free to visit the wellness center anytime during normal operating hours (5:30 AM until 10:00 PM). Participant adherence to the exercise intervention was assessed using an exercise log, which the participants completed for each exercise session. The log was checked daily by a study staff member. Participants were given written and oral feedback on their progress.

Results

Study Completion Rates

Approximately 200 adults inquired about participation in the study. Telephone screening determined preliminary eligibility for about half of these, and the first 60 who resided within an easy commuting distance from our facilities were scheduled for an initial appointment. After the elimination of those who did not show up for any of their appointments, as well as those who did not meet inclusion criteria (as detailed above), 43 participants were enrolled in the study. Of the 43, two did not complete the RLS Rating Scale at baseline and were excluded from participation. The remaining 41 participants were randomly assigned to either the exercise or the control group. Due to scheduling constraints, a delay of up to 4 weeks in contacting participants with exercise group assignment occurred. By this time, 13 (9 exercise and 4 controls) were no longer

available to participate for various reasons including changes in work schedule, injury, unresolved or worsening medical conditions, and relocation. Thus, the final sample that participated in assigned treatment groups and completed assessments at 6 weeks post assignment was 28: 11 exercise group participants and 17 controls. At 12 weeks, data were available for 11 exercise group assignees and 12 controls.

Initial analyses revealed no significant attrition bias. Those assigned to the exercise group were more likely than control group members to be unavailable for participation on notification of treatment group assignment (45% vs 20%, $P < .01$). However, those 13 unavailable when contacted did not differ significantly from the 28 available on RLS Rating Scale scores nor on any available demographic variables ($P > .05$). Additionally, those who participated for the full 12 weeks did not differ from those who participated for only 6 weeks on treatment group assignment, RLS Rating Scale scores, or on any demographic variables ($P > .05$).

Group Baseline Differences

Baseline demographic and basic physical and medical characteristics of the participants are presented in Table 1. The average age was 53 years. Although treatment group assignments were random, some differences between the two groups in baseline variables were evident. The exercise group participants were significantly taller than the control group. In addition, although not statistically signif-

Table 2. RLS Rating Scale Scores by Treatment Group

| RLS Score | Exercise Group (N = 11) | Control Group (N = 17) | t Test Value | P Value |
|----------------------|-------------------------|------------------------|--------------|---------|
| Baseline | | | | |
| Total severity score | 20.6 (6.4) | 22.5 (6.4) | 0.74 | .464 |
| Single item rating | 4.0 (1.8) | 4.2 (1.7) | 0.27 | .792 |
| 6 weeks | | | | |
| Total severity score | 12.6 (4.8) | 20.8 (7.4) | 3.27 | .003 |
| Single item rating | 1.7 (0.5) | 4.1 (1.8) | 4.21 | <.001 |
| 12 weeks | | | | |
| Total severity score | 12.1 (5.6) | 21.5 (6.3) | 3.75 | .001 |
| Single item rating | 2.0 (1.2) | 4.3 (1.3) | 4.48 | <.001 |

Note: Total severity scale scores range from zero to 40 with higher values being indicative of more severe symptoms. Single item rating is an ordinal scale with range of 1 to 8. Higher values are indicative of more severe symptoms. Cell values represent means (SD).

icant, there was a trend for exercise group participants to be more likely to be male and to be slightly heavier. However, none of these background variables was significantly related to any of the baseline RLS scores. Because of this and small sample size, analyses presented below did not include controlling for any of these factors. Before the study, 2 control group participants were on pramipexole (a dopamine agonist) and 2 exercise group participants were on the anticonvulsant gabapentin. Both of these medications have been shown to improve the symptoms of RLS. During the course of the study, no patients had changes in medications known to improve or exacerbate RLS symptoms. Furthermore, there was no significant difference between the 2 groups in baseline exercise frequency or energy expenditure based on the CHAMPS questionnaire.

Change in RLS Symptoms

A comparison of the exercise and control groups on RLS Rating Scale scores is presented in Table 2. The exercise and control groups did not differ significantly in either the total RLS severity total score or the 8-point rating at baseline. However, by 6 weeks, the exercise group scored significantly lower on both the total RLS severity score and the rating, indicating improvement of symptoms. Severity scores for the control group decreased less than 8% over 6 weeks, whereas exercise group severity scores dropped by 39% during the same time period. Scores for both groups remained relatively stable from six to twelve weeks, with symptom improvement from baseline only evident for the exercise group. One exercise group participant developed knee pain while participating in the ex-

ercise intervention. This required referral to an orthopedic surgeon.

In addition to the analyses presented in Table 2, factorial repeated measures MANOVAs were calculated to examine change in RLS scores over time by group status. The severity scores of the control group did not change significantly over time. The exercise group changed from baseline to week 6 [$F(2,9) = 84.0, P < .001$], but did not change significantly from week 6 to week 12. When the 2 groups were examined together, the group by severity score interaction was significant ($F = 7.74, P = .010$), indicating that the exercise and control groups differed significantly over time. The same pattern was observed for the rating scores. The control group did not change significantly over time. The exercise group changed from baseline to week 6 [$F(2,9) = 119, P < .001$], but did not change significantly from week 6 to week 12. When the 2 groups were examined together, the group by rating score interaction was significant ($F = 10.49, P = .003$), indicating that the exercise and control groups differed significantly over time. Analysis was by intention to treat.

Discussion

This is the first randomized controlled trial that we are aware of to examine the effectiveness of exercise in managing RLS symptoms. To date, nearly all treatment strategies for RLS have relied on pharmaceutical intervention. In this study, participation in aerobic and resistance exercise significantly reduced RLS symptom severity.

The improvement in RLS symptoms occurred as early as 6 weeks, similar to the time course of

common pharmaceutical treatments,^{12,22} and the reduction in RLS symptoms was maintained throughout the 3 month intervention period. Additionally, the improvement in RLS symptoms appeared to show a ceiling effect at 6 weeks, with no further significant improvement occurring. Again, this may be similar to pharmacological treatment, as in trials of pharmaceuticals for RLS, the response to treatment appears to be greatest at 6 to 12 weeks, with further treatment not providing additional reduction in symptoms.^{22,23}

Future studies are needed to further address the effects of exercise on the symptoms of RLS. The current study results are promising, but larger studies are necessary before exercise is routinely prescribed for RLS. Medications have documented benefit for RLS in large studies and remain the primary therapy for moderate to severe RLS. No attempts were made in this study to differentiate between the effects of aerobic and resistance training in the benefit observed. Future studies should evaluate the effectiveness of different types of exercise. This study did not attempt to correlate the improvement in RLS symptoms with the quantity of time exercising. Furthermore, we did not control for medication usage, although there were no changes in medications throughout the trial. Notwithstanding these limitations, the results are promising, particularly considering the numerous other advantages known to be associated with aerobic and resistance exercises, particularly cardiovascular, metabolic, and musculoskeletal.

Weaknesses of this study include small sample size, high attrition, and obvious inability to blind participants to their assignment group. Strengths of the study include randomization of participants, concealment of allocation, analysis by intention to treat, and patient-oriented primary outcome.

Conclusions

The findings of this study demonstrate that an exercise program consisting of a resistance and aerobic component was effective in improving symptoms of restless legs syndrome. No effort was made to discontinue medications that may exacerbate or improve RLS symptoms. As such, these findings support the use of exercise as an adjunct to treatment of RLS. Future studies should include larger cohorts, assess the efficacy of various types of exercise (ie, aerobic versus resistance), and should control for medication usage.

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