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Exercise Cynosure in Restless Leg Syndrome: A Scoping Review

Harshita Yadav¹, Anuradha Lehri², Manisha Uttam³

¹Harshita Yadav, MPT (Orthopedics), PhD Researcher, Punjabi University, Patiala, Assistant Professor, R.P. Indraprastha Institute of Medical Sciences, Karnal.

²Anuradha Lehri, PhD, Assistant Professor, Department of Sports Science, Punjabi University, Patiala

³Manisha Uttam, MPT (Neurology), PhD Researcher, Punjabi University, Patiala, Assistant Professor, R.P. Indraprastha Institute of Medical Sciences, Karnal.

Corresponding Author : Harshita Yadav, Address: Street no.5, Aryan agar, Ballour road, Bahadurgarh, Haryana.

ABSTRACT: Restless Leg syndrome (RLS) is a common neurological movement disorder usually involving motor restlessness in the lower limbs. It is frequently associated with rhythmic muscular jerks in lower limb called as periodic limb movements (PLMS). RLS can be primary which is idiopathic in nature or it can be secondary which is symptomatic in nature. The objective of the review is to find the exercise training programme which had been provided to RLS patients. The symptoms can be categorized as intermittent, daily or refractory. There is abundance of evidences regarding pharmacological and non-pharmacological treatments which are available for RLS patients. The exercise training programme has shown improvement in outcome measure such as functional quality, sleep quality, depression score, quality of life, exercise quality and symptoms severity. To our knowledge, there are only four experimental trails which had evaluated the effects of exercise training programme in RLS patients. There is a need to explore more on the effects of exercise training programme RLS patients.

Keywords: Ekbohm disease, Periodic limb movements, Training, Night walker's syndrome, Non-pharmacological.

INTRODUCTION

The "Restless Leg Syndrome" (RLS) termed was coined by a Swedish Neurologist Karl- Axel-Ekbohm in 1945, also known as Ekbohm Disease. It is a sensorimotor neurological disorder with the corestone of urgent demand of moving the legs with disagreeable leg sensations frequently during sleep hours. The sensations appear deep into the legs and rarely in arms ^[1].

The prevalence of RLS in adult's general population range between 5% and 8.8% ^[2]. Whereas, the prevalence of uremic RLS in End-stage renal disease (ESRD) population is found to be 30% ^[3]. Evidence shows that 18.5% of RLS subjects also had periodic limb movement disorder (PLMD). RLS increases with the age but not PLMD ^[4]. A study found that, women are more affected than men, studying Parity as a major factor for the gender difference in causing the RLS ^[5].

The purpose of this paper is to review the literature on role of exercise in RLS and to summarize the available training programmes, their implementation strategy; perceived and real benefits with the emphasis on the improvement in outcome measure.

To elucidate about RLS, a detailed history of patient complaint is to be taken as there is no biomarker, physical examination or radiological examination to depict RLS. A diagnostic criteria was introduced by International RLS study Group (IRLSSG) which had been updated in 2012 has near to similar criteria to DSM-5 criteria ^[6] in Table 1.

Table 1 DSM-5 specific criteria for RLS

- A. An urge to move the legs in a response to uncomfortable and unpleased sensations in legs, characterized by all of the following:
1. The urge to move the legs begins or worsens during periods of restoring activity.
 2. The urge to move the legs is partially or totally relieved by movement.
 3. The urge to move the legs is worse in the evening or at night than during the day, or occurs only in evening or at night.
- B. The symptoms in Criteria A occur at least three times per week and have persisted for at least 3 months.
- C. The symptoms in criteria A are accompanied by significant distress or impairment in social, occupational, educational, academics, behavioral, or other important areas of functioning.
- D. The symptoms in criteria A are not attributable to another mental disorder or medical condition (such as arthritis, leg edema, peripheral ischemia, leg cramps) and not better explained by a behavioral condition (positional discomfort, habitual foot tapping).
- E. The symptoms are not attributable to physiological effects of a drug abuse or medication.

Primary and Secondary RLS

Primary RLS cause is not known, therefore also known as idiopathic RLS. This type of RLS has genetic basis and is largely seen to run in families. It usually seems to occur before age of forty years [7]. Secondary RLS type is also known as symptomatic RLS. It is found to be associated with many neurological conditions (axonal neuropathy, parkinson’s disease, spinocerebellar ataxia); medical conditions (anemia, pregnancy, ERDS, rheumatic disease, uremia, vitamin B₁₂ deficiency, fibromyalgia, hypothyroidism, varicose veins, folate and magnesium deficiency, sjogren’s syndrome) and drugs (antihistamines, anticonvulsants, dopamine antagonists, anti-

depressants, antipsychotics, beta-blockers, caffeine, lithium) [1].

Clinical Features

Most of the patients get out of bed and walk around in order to produce a physical activity depending upon the level of symptoms they are dealing with, therefore RLS is also known as Night walkers’ syndrome [1]. A common subjective feeling for restless leg syndrome is briefly termed in Table 2 [1,7,8].

Table 2 Different sensations in Restless leg syndrome

- Creepy-crawly
- Ants crawling
- Jittery
- Pulling
- Worms moving
- Soda bubbling in the veins
- Electric current
- Shock-like feelings
- Pain
- The gotta moves
- Burning
- Jimmy legs
- Heebie jeebies
- Tearing
- Throbbing
- Tight feeling
- Grabbing sensation
- Elvis legs
- Itching bones
- Crazy legs
- Fidgets
- Rubbing
- Kneading
- Groaning
- Paraesthesias deep in legs

Furthermore, there are three supportive clinical and three associated features of RLS are listed in Table 3 [3,9].

Table 3 Supportive and Associated clinical features

<p>Supportive Features</p> <ul style="list-style-type: none"> • Sleep disturbance • Periodic leg movements • Response to dopaminergic therapy • Family history • Normal medical/physical evaluation <p>Associated Features</p> <ul style="list-style-type: none"> • Onset can be at any age, patients are usually middle aged or older at presentation Leg discomfort or need to move result in insomnia • Low serum ferritin(< 50 µg/L) • The natural clinical course of the disorder is in general chronic and • Progressive • Medical evaluation and physical examination (mainly used for idiopathic patients and not for secondary restless legs syndrome patients)

The symptoms can be intermittent, daily basis or refractory in nature^[10].

Intermittent RLS

The condition is bothersome when present, requires entailment considerations for resolving by treatment but does not frequently require attention on daily basis.

Daily RLS

The condition is troublesome to patients with moderate to severe symptoms and needs a daily therapy to abide the treatment effects. Patients usually compromise their quality of life everyday or on most days of the week.

Refractory RLS

The condition is refractory as daily symptoms are not responding to treatment with drugs (dopaminergic and non- dopaminergic) and are managed under special sleep specialists considerations.

Management

RLS is condition which is managed both with pharmacological and non-pharmacological treatments. A cross-over design by Saletu et al. suggests that clonazepam significantly improved objective sleep efficiency and subjective sleep quality in RLS patients^[11]. An American Academy of sleep medicine clinical practice guideline in its systematic literature and meta-analysis has updated the pharmacotherapy treatment with standard level of recommendation (pramipexole and ropinirole), guideline level of recommendation (lenodopa with opioids, gabapentin) and option level of recommendation (Pregabalin, Clonidine, iron supplementation)^[12].

There are abundance of evidence for the use of pharmacological treatment in RLS which avenue each drug with its dosage and agumentation for its efficacy^[13-15]. Seeking evidence towards non-pharmacological treatment mainly addresses a good sleep hygiene, hot or cold massage, stretching, mental activities, reducing caffeine and alcohol consumption, pneumatic compression devices, near -infrared light exposure, complementary vitamin (Vit. B, Vit. E, Vit. B₁₂, Vit. D, Folic acid, zinc, Glucosamine), behavioral therapy, acupuncture and physical activity has set basis for the patients with RLS. Also, iron supplementation is effective in patients with iron deficiency or refractory RLS^[1, 9, 12, 15- 17].

Affirming Exercises training in restlessness leg syndrome

The current literature had found four experimental trails (a pilot study, a randomized clinical trial, a randomized control trial and a randomized comparative study) in total to find the effectiveness of exercise in treating RLS patients^[18-21].

Sakkas et al. presented the first pilot study, to see the influence of exercise training in RLS patients who were trained during hemodialysis (HD) procedure. A 16 weeks aerobic exercise training was given to fourteen patients on HD. Subjects with mean age 59±16 years with untreated RLS were assigned to exercise group (n=7) and control group (n=7) according to their will. The aim of the study was to compare international RLS study

group scale (IRLSSG), functional ability, and quality of life at baseline and after 16 weeks. Exercise training regime includes 45 minutes continuous cycling using a beside cycle ergometer. The exercise resistance was set between 65% and 75% of their maximum power capacity (watts) which was noted both at baseline and after 16 weeks and was readjusted every 2 weeks by submaximal cycling test. Also, each training session included 5 minutes warm up and 5 minutes cool down periods. According to American college of sports medicine (ACSM) guidelines, blood pressure and heart were monitored constantly after 16 weeks of exercise training programme score reduced by 42% ($p=0.002$) with improvement in functional ability ($p=0.02$), exercise capacity ($p=0.01$), quality of life ($p=0.03$), sleep quality ($p=0.001$). Aerobic exercise training is safe line of treatment in patients with RLS symptoms with patients on HD giving a suggest time path to find more associated link ups between exercise training program and RLS patients ^[18].

Aukermann et al. conducted a first randomized controlled trial, evaluated the effectiveness of exercise programme on idiopathic RLS, whose severity was milder than in other trials with medications. 28 subjects were randomly assigned to exercise ($n=11$) and control ($n=17$). A 12 week conditioning programme of aerobic and lower-body resistance training, 3 days per week was given to exercise group. Exercise intervention consists of walking for 30 minutes, 5min warm up- and cools down, at 40% to 60% of age predicted maximum heart rate. Patients were instructed to perform one set of 8 to 12 repetitions of each exercise for first 2 weeks with progression increased to 2 sets strength training activities includes horizontal leg press, leg extension, leg curl, hip adduction, hip abduction and seated rotatory calf press IRLS was evaluated at baseline, 6 weeks and 12 weeks of exercise programme. After 12 weeks, exercise group showed significant improvement in symptoms with ($p=0.001$) for IRLSSG than control group ^[19].

A single blind randomized controlled trial by Giannaki et al. had provided the progression exercise training programme in uremic RLS. Twenty four subjects were randomly allocated to

two groups: exercise group ($n=12$): control exercise with no resistance ($n=12$). The exercise session in both groups included intradialytic cycling for 45 min at 50 rpm. Resistance was applied to progressive exercise training group at 60-65% of maximum exercise capacity. The IRLSSG severity scale, functional capacity and daily sleepness status were assessed at baseline and 6 months after training programme. Symptoms severity was reduced by 58% in progressive exercise training group ($p=0.003$) with improvements in functional capacity ($p=0.04$), sleep quality ($p=0.038$) and depression score ($p=0.000$) in uremic RLS ^[20].

Another 6-month, placebo-controlled comparative study by Giannaki et al in uremic RLS was conducted to compare the effect of exercise training and dopamine agonists. Subjects were randomly assigned to exercise training group ($n=16$); dopamine agonist group ($n=8$) and placebo group ($n=8$). The exercise program was for 3 times per week during HD session. The exercise intensity was readjusted on monthly basis. The analysis after 6-month exercise training program was effective in reducing symptoms by 46% ($p=0.009$); whereas dopamine agonists reduces the symptoms by 54% ($p=0.001$), there was a significant improvement in quality of life ($p<0.005$) in both the groups ^[21].

Mechanism

The possible reasons on the basis of which exercise training program showed improvement in RLS patients may be the increment in endorphin levels following exercise program are endogenous opioids polypeptide compounds produced by pituitary gland and hypothalamus produce analgesia and a sense of well-being ^[22].

The type of exercise or activities in intermittent and daily RLS is almost same, such as mental altering activities (video games or cross puzzles) to reduce symptoms at times of boredom, but in refractory RLS it is still not evident ^[23].

Conclusion

The recent literature review had shown the improvement in outcome measures associated with RLS, but still there is meagerness of

evidences on the effectiveness of different exercise and training programmes in RLS patients. Therefore, there is a need to explore more experimental trials to evaluate the exercise program for reinforcing the treatment in RLS patients.

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