Sleep Medicine 17 (2016) 99–105

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Review Article

Alternative treatment of restless legs syndrome: an overview of the evidence for mind–body interventions, lifestyle interventions, and neutraceuticals

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ARTICLE INFO

Article history:
Received 27 July 2015
Received in revised form 16 September 2015
Accepted 22 September 2015
Available online 3 December 2015

Keywords:
Restless legs syndrome
RLS
CAM

ABSTRACT

Conventional pharmacologic treatment of restless legs syndrome (RLS) may be limited in some people. Up to 65% of patients with RLS regularly use alternative practices for symptom relief. We reviewed the current clinical evidence, and we proposed physiologic basis for various alternative practices for RLS including mind–body interventions (conventional exercise, yoga, and acupuncture), non-pharmacologic lifestyle interventions (pneumatic compression devices [PCDs], light therapy, and cognitive–behavioral therapy [CBT]), and neutraceuticals (vitamins, valerian, and Chinese herbs). Based on the available evidence, regular physical activity should be recommended for the treatment of RLS symptoms. Oral iron supplementation should be considered for people with RLS who have low ferritin levels, although criteria to identify probable responders, and optimal formulations and durations of treatment are needed. Supplementation for low levels of vitamins E, C, and D could be considered, although evidence specifically in RLS is limited, and it is unclear if levels should routinely be checked in patients with RLS. Insufficient evidence exists for yoga, acupuncture, PCDs, near-infrared light therapy, CBT, valerian, or Chinese herbs, but preliminary studies on each of these suggest that high-quality randomized controlled trials may be warranted to support and verify the data presented.

1. Introduction

Restless legs syndrome (RLS) is a neurologic disorder characterized by an uncomfortable urge to move the limbs. Symptoms typically occur when a person is resting, may be alleviated with movement, and occur at night in a circadian pattern, which can significantly disrupt sleep. The prevalence of RLS may be anywhere from 10% to 40% of adults depending on age, geography, and comorbid conditions [1,2], and reduction in the quality of life due to RLS symptoms is significant [1,3,4]. RLS symptoms are associated with poorer sleep, greater risk of anxiety and depression [5], poorer overall health status, and greater economic burden. The goal of RLS treatment is symptomatic relief and improved sleep quality. Pharmacologic therapies are considered the treatment of choice for RLS, and they include dopamine agonists, anticonvulsants, and benzodiazepines. These agents have the strongest evidence for symptomatic benefit in RLS, although the adverse effect profile and potential for augmentation and refractory symptoms, particularly with dopamine agonists, may limit use in some people. As a result, many patients suffering from RLS symptoms turn to complementary and alternative (CAM) treatments for symptomatic relief. CAM treatments include a diverse group of medical therapies, practices, and products that share in common their exclusion from conventional Western medicine practices and teachings. CAM therapies are tied together by a focus on individuality over typology, a holistic approach to wellness, and an emphasis on the importance of patient empowerment in the healing process. According to a 2004 survey by Cueller et al., up to 65% of patients with RLS use CAM practices regularly to relieve symptoms of RLS [6].

The National Center for Complementary Alternative Medicine (NCCAM) classifies CAM interventions into the following groups: (1) mind and body practices such as acupuncture, massage, meditation, movement therapies, relaxation techniques, Tai Chi, and yoga; (2) alternative systems such as traditional Chinese medicine (TCM), Ayurvedic medicine, and homeopathy; and (3) natural products such as herbals, vitamins, minerals, and probiotics. According to Cueller [6], the most commonly used modalities among patients with RLS were vitamins, exercise, prayer, and meditation. Unfortunately, clinical and physiologic evidence for the benefits of these interventions are lacking, and evidence-based guidelines such as those from the

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http://dx.doi.org/10.1016/j.sleep.2015.09.009
1389-9457/

American Academy of Sleep Medicine (2012) clearly state that these various interventions cannot be recommended for the treatment of RLS [7]. In the following, we review the current clinical evidence for various CAM practices in RLS including mind–body interventions, non-pharmacologic lifestyle interventions, and neutraceuticals.

2. Mind–body interventions

Lifestyle interventions, which promote general health and improved circulation and cardiovascular health, are suited to the treatment of RLS based on the vascular theory of the disease. This theory proposes that lower extremity micro-ischemia may be responsible for the symptoms of RLS [8,9]. This is supported by the association of RLS symptoms with sedentary lifestyle and medical comorbidities such as obesity and peripheral neuropathy, the characteristic improvement in symptoms with leg movement, and the association of RLS with chronic venous disorders in which the prevalence can be as high as 36% of patients [10]. Others have proposed that RLS symptoms may originate from reduced supraspinal inhibitory signals originating from hypothalamic dopaminergic neurons [11]. Stretching and resistance exercise have been proposed to impact these neural pathways [12], although it is unclear to what extent the influence of mind–body interventions on cerebrospinal chemistry may impact these processes. Endorphins likely also impact these supraspinal pathways, and opioids have been used with some success in RLS. Notably, both dopamine and opioids are thought to be involved in the placebo response, and a meta-analysis by Fulda et al. demonstrated a placebo response in RLS patients as high as 40% for severity scale reporting [13], underscoring the importance of well-designed studies in this population. Thus, alternative interventions that impact central nervous system (CNS) dopamine and endorphins, among other neurotransmitters, are interesting and complicated candidates for investigation in the treatment of RLS symptoms.

2.1. Conventional exercise

Structured physical activity aims to improve strength and cardiovascular health. As medical comorbidities and sedentary practices have been associated with RLS, several studies have looked at the impact of physical activity on RLS symptoms. Some authors have proposed that exercise reduces the risk of comorbid conditions, which act as risk factors for RLS [14,15]. Others have proposed that exercise impacts RLS by improving circulation or through the release of endorphins, which improve mood and pain [15–17]. In a case series of 13 subjects, Dinkins et al. demonstrated that straight-leg raise stretching maneuvers were associated with a 63% reduction in RLS symptom severity [12]. There are five interventional studies examining the effects of exercise in patients with RLS (Table 1) [14,15,18–20]. Four of these studies are randomized controlled trials (RCTs), but only one of these studies was in a primary, non-uremic population [14]. Each of the studies demonstrated that exercise was beneficial for RLS symptom severity, but the studies were less consistent with regard to improvement in sleep or quality of life outcomes. In most cases, RLS symptom severity is rated using the International Restless Legs Syndrome Study Group Severity Scale (IRLSSG), a validated RLS rating scale [21]. In the non-uremic RLS study, which comprised 28 RLS participants, RLS symptom severity was significantly reduced at six weeks by 39% in the exercise group (which included aerobics and lower extremity resistance exercises) compared with only 8% reduction in the control group. The difference persisted at 12-week follow-up [14]. Similar benefits were seen in studies of patients with uremic RLS. Giannaki et al. studied 24 uremic RLS patients over six months, and they found that the type of exercise was important; aerobic exercise with progressive

Table 1
Summary of Exercise Studies in RLS.

Study	Design	*N*	Population	Intervention	Control	Duration	Primary Results	Other Findings
Aukerman, 2006 [14]	RCT	28 (11 exercise, 17 control)	Primary RLS	Treadmill walking × 30 min at 60% max predicted HR + low-intensity leg strength training	Instructed in lifestyle interventions (tobacco, alcohol, caffeine, sleep hygiene)	12 weeks (3×/week)	Exercise: 39% ↓ IRLSSG at 6 weeks; Control: 8% ↓ IRLSSG at 6 weeks; ($p = 0.003$, maintained at 12 weeks)	
Sakkas, 2008 [18]	Nonrandomized clinical trial	14 (7 per group)	RLS with nephropathy on HD >6 months	Cycling × 45 min during HD with resistance at 65–75% max power capacity	No intervention	16 weeks (3×/week)	Exercise: 42% ↓ IRLSSG at 16 weeks ($p = 0.02$); Control: No change in IRLSSG at 16 weeks	Self-rated functional ability, exercise capacity, QoL, and sleep quality all improved in exercise group only.
Mortazavi, 2013 [19]	RCT	26 (13 per group)	RLS with nephropathy on HD >3 months	Cycling × 30 min during HD	No intervention	16 weeks (3×/week)	Exercise: −5.5 (±4.9) points at 16 weeks; Control: −0.5 (±2.3) points at 16 weeks ($p = 0.003$)	No significant difference in QoL rating
Giannaki, 2013 [15]	RCT	32 (16 exercise, 8 ropinirole, 8 placebo)	RLS with nephropathy on HD >3 months	Cycling × 45 min at 65% max exercise capacity	Ropinirole 0.25 mg or placebo nightly	6 months (3×/week)	Exercise: 46% ↓ IRLSSG at 6 months ($p = 0.009$); Ropinirole: 54% ↓ IRLSSG at 6 months ($p = 0.001$); Placebo: 5% ↓ IRLSSG at 6 months ($p = 0.732$)	QoL ratings improved in exercise and Ropinirole groups. Sleep quality rating improved only with Ropinirole.
Giannaki, 2013 [20]	RCT	24 (12 per group)	RLS with nephropathy on HD >3 months	Cycling × 45 min at 65% max exercise capacity	Cycling × 45 min without resistance	6 months (3×/week)	Intervention: 58% ↓ IRLSSG at 6 months ($p = 0.003$); Control: 17% ↓ IRLSSG at 6 months ($p = 0.124$)	Depression and sleepiness ratings were significantly improved in intervention group over control.

Abbreviations: RCT = randomized controlled trial; IRLSSG = International Restless Legs Syndrome Study Group Severity Scale; QoL = quality of life.