Sleep-Related Leg Cramps
A Review and Suggestions for Future Research

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KEYWORDS

• Sleep • Leg cramps • Quinine • Continuous positive airway pressure • Statins • Elderly • Children • Pregnancy

KEY POINTS

- Leg cramps are a common cause of sleep disruption and may be the most common sleep disorder.
- There are medications and behavioral treatments for sleep-related leg cramps, although the evidence is poor for all but quinine. Quinine is useful for leg cramps, but dangerous.
- There are numerous secondary causes of sleep-related leg cramps, although the emphasis is on idiopathic sleep-related leg cramps.
- Long-acting β-agonists may be the drug type most strongly associated with sleep-related leg cramps, with statins not being as commonly associated as some have believed.
- Because leg cramps are so common, future research into sleep-related leg cramps is important, and a standardized questionnaire would greatly facilitate this.

Sleep-related leg cramps (SRLCs), also called nocturnal leg cramps, have been insufficiently studied. The lay term is a Charley horse. However, the origin of the term remains obscure. SRLCs have also been called rest cramps in the Canadian literature.[1] In this article, the essential features of the condition, the prevalence, and the differential diagnosis are described, the primary and secondary associations and treatment effects are discussed, and opportunities for further research and education are suggested. This review is not primarily evidence based because the subject has not been well studied for a variety of reasons, and only in the cases of some treatment options are there any evidence-based data. In addition, the author has added his own anecdotal information from his patients with leg cramps, and that of his own experience with leg cramps.

The *International Classification of Sleep Disorders, Third Edition, 2014* describes 3 diagnostic criteria for SRLCs. These criteria include "a painful sensation in the leg or foot associated with sudden, involuntary muscle hardness or tightness, indicating a strong muscle contraction; the painful muscle contractions occur during the time in bed, although they may arise from either wakefulness or sleep; and third, the pain is relieved by forceful stretching of the affected muscles, thus releasing the contraction."[2] Often, the coping strategy involves getting out of bed to put weight on the afflicted limb.[3] Nocturnal cramps are generally in the calf or muscles in the foot and rarely include the thigh muscles. The cramp is sometimes preceded by an early warning tightening sensation and sometimes can be prevented by dorsiflexing the foot, according to the author's patients. The other essential feature of SRLCs is that they disturbs sleep. Some individuals have multiple leg cramps nightly, whereas others have only the occasional SRLC. If cramps are severe, there

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may be residual tenderness and soreness in the muscle for 1 to 2 days. In addition to the obvious diurnal variation, there is some evidence of a seasonal variation, with more quinine being prescribed for leg cramps in the midsummer as opposed to midwinter in a Canadian study.[4]

SRLCs may be idiopathic or secondary to metabolic or other medical disorders. The most common type is probably idiopathic or this may reflect our incomplete knowledge of etiopathology. Secondary associations have included pregnancy,[5] peripheral vascular disease,[6] hypokalemia,[1] hypocalcemia,[7] hypomagnesemia,[8] spinal stenosis[9] dialysis,[10] dehydration and other electrolyte disturbances,[11] other metabolic disorders including metabolic syndrome,[12] and diabetes mellitus, although 1 study[6] suggested no correlation between diabetes and leg cramps. Various drugs have also been associated with the condition (to be discussed later). In addition, prolonged standing has been associated with both nocturnal leg cramps and varicose veins.[13]

PREVALENCE

The prevalence is unclear, but it is clear that SRLCs are common. Some studies have suggested that 50% to 60% of the adult population[6,14] may experience SRLCs and some children also experience them.[15] In general, SRLCs are increasingly common with advancing age, although they have been reported in another study in children as young as age 8 years.[15] That study showed a 7% prevalence in children 8 years or older although the frequency of cramps was low by adult standards. It is not clear that there is a gender predominance, although some studies have suggested a greater prevalence in females.[14] The frequency of this disorder within individuals varies considerably. In the author's opinion, leg cramps are rarely the primary reason for a sleep medicine referral or self-referral. The perception of many patients seems to be that SRLCs are just an unpleasant part of getting older and many may not recognize that treatments are available. This attitude of the patient may also be another reason why SRLCs have not been thoroughly studied. There is no clear evidence of familial pattern thus far. Pregnant women may be more likely to have SRLCs, which normally resolve after delivery. Estimates are that between 30% and 45% of pregnant women have SRLCs.[5,16]

The author's own unpublished data from his busy sleep medicine practice show that only 2.3% of patients interviewed for the first time reported a problem with leg cramps. This finding included 75 patients of 3257 patients who had been interviewed and examined between January, 2011 and December, 2014. Clearly, this is not a measure of prevalence but may suggest certain things about patients' willingness to bring up the problem voluntarily. Another factor is that patients often come to see the sleep specialist for a more severe sleep disorder, and there may not be time to investigate SRLCs from both the clinician's and the patient's viewpoint.

DIFFERENTIAL DIAGNOSIS

In discussing leg cramps with patients, it seems that some do not differentiate well the distinctions between restless legs syndrome (RLS) and SRLCs; however, the determination should be easy for the clinician if one keeps in mind the sudden nature of SRLCs versus the gradual and persistent effect of RLS. In general, the patient with SRLC describes a tightened or cramped muscle, which the pure RLS case does not describe. Dystonias can be confused with SRLCs but involve agonist versus antagonist simultaneous muscle activation. RLS is difficult for the patient to describe, whereas SRLCs are specifically described. Also, leg cramps are not expected to be alleviated with dopaminergic agonists. Dystonias generally are not relieved by stretching or standing on the affected limb, as are SRLCs. In general, the phenomenologies are distinct. It may be that RLS and SRLCs cluster together in the same individuals, and that may be 1 reason why the patient seems to often confuse these 2 conditions. Growing pains in children can be differentiated by their lack of sudden onset. Secondary causes of leg cramps are probably rarer than idiopathic. The primary focus of this review is the idiopathic leg cramp.

Muscular pain fasciculation syndrome has been described and involves muscular aching, fasciculations, fatigue, and paresthesias.[17] It is not more or less prominent during sleep and does seem to be a rare disorder. Like SRLCs, it is worsened by exercise, but unlike SRLCs, the symptoms subside at rest generally. Various myelopathies may mimic the condition, but once again, these are more likely to occur with muscular effort and not at rest, as do leg cramps generally. A similar disorder was described[18] called cramp fasciculation syndrome, which seems to be a peripheral nerve disorder. Fibromyalgia has been believed to be associated with both leg cramps and RLS in the literature,[19] but clearly, more study is needed to determine degree of overlap.

Secondary Sleep-Related Leg Cramps

Leg cramps while awake during the day may have the same etiopathology as SRLCs, but this has not

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