Diagnosis and treatment of nocturnal leg cramps

Nocturnal leg cramps are very common in elderly people. Diagnosis and treatment of any underlying causes such as myositis is important. Physiological treatments such as massage and exercise have not been thoroughly investigated, and the main drug treatment is quinine.

Dr Gary Pratt* Specialist Registrar Department Geriatric Medicine, Sheffield University Teaching Hospitals, Barnsley NHS Foundation Trust, Gawber Road, Barnsley S75 2EP, UK.
Dr Ahmed H Abdelhafiz Consultant Geriatrician, Rotherham General Hospital, Moorgate Road, Rotherham, S60 2UD, UK.
***email** gary@docs4.wanadoo.co.uk

Nocturnal leg cramps are painful involuntary muscle contractions that occur when the patient is recumbent. They are a very common complaint in elderly people. Careful history taking, physical examination, and routine investigation may help in establishing a diagnosis of idiopathic leg cramps whilst simultaneously excluding other serious conditions such as myositis. Current evidence regarding potential causes and treatment is limited to small studies and expert opinion. Physiological treatments including stretching, massage, and walking have had little investigation.

Quinine is generally regarded as the most effective available pharmacological treatment. Some trials have looked into alternatives to quinine treatment, but most of the trials investigating drug treatment for nocturnal leg cramps in elderly patients have studied the efficacy of quinine. Interestingly, the results of these studies have been mixed despite similar populations of patients, and treatment is not without risk. We discuss the evidence for quinine as well as for other potential treatments.

Epidemiology

A general population study published in 1994 found an overall prevalence of night cramps of 37%.[1] In this study, rest cramps were most commonly experienced in the muscles of the legs (83%), symptoms were present at night in 73% of patients, and the average episode lasted up to 9 minutes. About 40% of people in the study had cramps at least three times per week. In another study published in 1999, the prevalence of cramps was as high as 50% in the elderly population. A slightly higher prevalence has been reported in women.[2]

Pathophysiology

The pathophysiology of leg cramps remains unclear. Over the years various hypotheses have emerged. The squatting hypothesis suggests that we are at risk of developing cramps as a direct result of modern high sitting positions which can lead to muscle and tendon shortening.[3] At the end of the 19th century the belief that muscle cramps represented a psychosomatic disorder was widely held, and during the early 20th century vascular insuffiency was proposed as a major factor in developing cramps.[4]

Modern pathophysiological concepts, however, based around electromyographical studies suggest that cramps have a neural origin—spinal disinhibition or hyperexcitability of intramuscular terminal motor axons.[4,5]

Aetiology

In the majority of patients, leg cramps remain idiopathic in nature. Numerous potential causative factors have been reported. It is well recognised that patients receiving haemodialysis for chronic renal failure are prone to developing cramps, especially when dialysis is frequent. Additionally, patients with cirrhosis are known to have a higher incidence of leg cramps.[2]

Other medical conditions linked to the development of cramps include diabetes mellitus and hypothyroidism, as well as electrolyte disturbances such as hypomagnesaemia, hypocalcaemia, and hypokalaemia. The presence of

vascular insufficiency is reported as increasing the risk of developing cramp by up to three times. A link has also been demonstrated between arthritis and cramp development.[2,4] Several drugs have been implicated as causal in leg cramp development including diuretics, β-agonists, calcium channel blockers, statins and lithium. [6]

Differential diagnosis

All reviews suggest that the best diagnostic approach to leg cramps is taking a thorough history, and careful physical and neurological examination.[7,8] The differential diagnosis of leg cramps is wide with numerous conditions that can present in a similar way, including:

- Muscle strain
- Deep vein thrombosis
- Ruptured Baker`s cyst
- Claudication
- Radiculopathy
- Myalgias (eg, fibromyalgia, exertional)
- Restless legs syndrome
- Periodic limb movement disorder

Treatment

After diagnosis, giving the patient a careful explanation and reassurance regarding the relatively benign nature of the disorder is helpful. Treatment of any underlying disorder is recommended. Consideration should also be given to withdrawal of medication associated with development of leg cramp. General advice regarding sleep hygiene, maintaining hydration, and stretching exercises to relieve cramps should be given to the patient.

Non-pharmacological treatment

Simple physiological methods should be tried in the first instance. Patients can easily be taught stretching exercises to relieve cramps. Advising patients with regards to leg posture when sleeping may also help. For example, placing feet on a pillow whilst sleeping on their back, or hanging feet over the end of the bed whilst sleeping on their front.

Stretching exercises undertaken during the day are commonly advised although there is a lack of good research evidence of effectiveness. In 1979, Daniell treated 44 patients with a passive calf muscle stretching regimen. After 24–72 hours, 21 patients reported disappearance of their symptoms and all reported cure within a week.[9] However, the study was not controlled and the results have never been replicated. In 2005, a randomised controlled study suggested that calf-stretching exercises were not helpful in reducing the frequency or severity of nocturnal cramps.[10]

Pharmacological treatments

Pharmacological treatment is recommended as second-line treatment. Several drugs have been used to prevent muscle cramp, although perhaps the best studied is quinine.

Quinine

Quinine is conventionally believed to be the best drug for the treatment of muscle cramps. Quinine is a white crystalline alkaloid powder obtained from the bark of the cinchona tree in South America. Since 1944 it has been commercially synthesised from coal tar. Multiple trials have been published regarding the efficacy of quinine in treating night cramps, but the evidence has been conflicting. The first meta-analysis of quinine's efficacy was published in 1995[11] and concluded that it significantly reduced the number of cramps over a 4 week period by 8·83 (95% CI 4·2–13·5) when compared with placebo. This represented a 27·4% reduction in the frequency of night cramps. Three years later,[12] the same authors produced a second meta-analysis, this time including unpublished data, and despite remaining significant, the reduction in cramps fell to 3·6 (95% CI 2·2–5·1) compared with placebo. No difference was noted in the severity or duration of cramps.

In a study published in 1991, quinine in combination with theophylline produced a greater reduction in cramp frequency than both placebo and quinine alone.[13] However, more than 65 years since its first reported benefits in the treatment of muscle cramps, quinine's use still remains controversial due to the concern over its risk:benefit ratio. Because of concerns regarding its safety, over-the-counter marketing of quinine was halted in the USA in 1995. The sustained use of a potentially harmful drug for what is essentially a benign condition remains debatable.

Other treatments

Magnesium salts have been looked at in two small studies, which showed reasonable evidence that such treatment may be of benefit in pregnant women, but no real evidence that it helped in idiopathic night cramps when compared with placebo.[14,15]

A randomised, double-blind, placebo-controlled study evaluated the safety and efficacy of vitamin-B complex in 28 elderly patients. 86% of the patients taking vitamin B had prominent remission of leg cramps at 3 months.[16] Another controlled randomised double-blind study

evaluated the frequency and severity of leg cramps in 40 patients on dialysis with a history of leg cramps receiving quinine and vitamin E (400 iu). Vitamin E treatment was associated with a 1 month reduction in leg cramp frequency which was sustained at 2 months.[17]

A small placebo controlled trial showed that naftidrofuryl oxalate may increase the number of cramp free nights by a third.[18] A further study suggested that orphenadrine citrate could reduce the frequency of night cramps by 30% in 90% of the 59 participants in a double-blind crossover trial.[19] Verapamil 120 mg at night was used in one uncontrolled study with seven of eight people reporting an improvement in their symptoms.[20]

Conclusion

Nocturnal leg cramps are common among older people. They can lead to sleep disturbance and have a profound negative impact on patients' quality of life. The differential diagnosis is wide and a thorough history taking and examination are therefore essential. Many common diseases and medications are associated with cramps, and any treatable causes should be sought and managed appropriately.

Simple physiological treatments should be considered as first-line treatment, and only if they fail should drug treatment be considered. By far the most studied drug treatment is quinine. Meta-analysis suggests that it is at least moderately effective in reducing the frequency of night cramps, but has no effect on the severity or duration of the cramps. When prescribing quinine we should be aware that we are prescribing a potentially harmful drug for what is essentially a benign condition and appropriate follow-up is required. A 4–6 week trial might be useful. The evidence for other medications is neither strong nor abundant, but consideration should be given to the prescribing of naftidrofuryl, orphenadrine, verapamil, or vitamins E or B complex, but further studies are needed for these therapies.

We have no conflict of interest.

Key points:

- Nocturnal leg cramps are common, affecting up to half of older people, and have significant impact on quality of life
- Physicians need to exclude and treat common causes of leg cramps before labelling them as idiopathic
- Physiological, non-pharmacological methods should be tried before drug therapy
- Quinine is the most commonly used drug but it has only modest effects and can have side-effects
- Controlled trials are needed to establish the benefit of physiological non-pharmacological therapies

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