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Nocturnal leg cramps: a snapshot summary

Key messages

- There is a lack of consensus about the definition of cramp;
- There are body sites where it occurs more commonly than others;
- Cramps can occur at any time of the day but are more common at night;
- Cramp can occur in both adults and children although it is reported more commonly in adults;
- A range of different comorbidities can be associated with cramp so good case history taking is vital to rule out causes which require referral for further investigation;
- Some medications cause cramp, so patients will need to have medication reviewed by their doctor;
- Non-pharmacological management of cramp has been described in various studies. These may be helpful for some patients who do not tolerate well pharmacological interventions.

Background

Cramp can occur in any muscle but there are a number of places in the body where it presents more commonly including the lower leg, thigh and foot. The focus of this

article is on nocturnal leg cramps. There is a lack of consensus about the definition of nocturnal leg cramps. The criteria below are based on those from the International Classification of Sleep Disorders (American Academy of Sleep Medicine, 2014) and include:

- The patient has a complaint of a painful sensation in the leg that is associated with muscle hardness or tightness.
- Recurrent awakenings from sleep are associated with painful leg sensations.
- The discomfort is relieved by local massage, movement, or application of heat.
- Polysomnographic monitoring demonstrates increased electromyographic activity in the affected leg and an associated awakening. No underlying medical disorder accounts for the sensation.
- Other sleep disorders may be present but do not account for the symptom.

While more commonly occurring at night, cramps can occur during the day also. A seasonal variation has been noted by some authors with a marked increase in symptom presentations found in summer compared with winter months in both Australia and Canada (Garrison *et al*., 2015).

Population

No difference in incidence has been found between men and women (Oboler *et al.,* 1991; Naylor and Young, 1994; Monderer *et al.,* 2010). Symptoms are reported more commonly in adults than children, and the presentation of symptoms in children is slightly different. Cramps in children typically last for about two minutes; they may occur once or several times per year starting from age eight and peaking around age 17. An incidence of 7.3% has been reported (Rabbitt *et al.,* 2016). In adults, cramp is more commonly reported in older age groups and increasing with age (Oboler *et al.,* 1991; Naylor and Young, 1994; Monderer *et al.,* 2010). Pregnancy is also a time when an increase in cramps is reported with 33-50% of women reporting symptoms which can increase in severity as pregnancy progresses (Young and Jewell, 2002; Hensley, 2009; Zhou *et al.,* 2015).

Pathophysiology

Spontaneous discharge of motor unit action potentials at a rapid and much higher rate than involuntary contractions is thought to result in symptoms of cramp (Rabbitt *et al.,* 2016). In older patients, loss of motor neurons is more pronounced and may contribute to the increased occurrence of leg cramps.

Comorbidities/differential diagnosis

A range of different comorbidities and underlying causes can be associated with symptoms of cramp: a selection of these are included in Table 1.

Table 1: Systems and conditions associated with the presentation of nocturnal leg cramps

System involved	Physiological conditions or named disorder
Neurological	Spinal stenosis Parkinson's Disease Motor Neurone Disease Dystonia Multiple sclerosis Neuropathy Radiculopathy Small-fibre sensory neuropathy
Endocrine	Diabetes mellitus Hypothyroidism Hypoadrenalism
Vascular	Peripheral vascular disease Venous insufficiency Chronic venous disease
Metabolic	Hepatic failure Chronic kidney disease,
Fluid/electrolyte disorders	Hypokalaemia Hyperkalaemia Hypocalcaemia Hyponatraemia Hypomagnesaemia Haemodialysis Acute volume depletion (Rabbitt *et al.,* 2016)
Other causes	Vitamin deficiencies Exercise Coffee Obstructive sleep apnoea
Pharmacological	Diuretics, inhaled long-acting beta 2 agonists, statins, nifedepine, acetylcholinesterase inhibitors, steroids, morphine, cimetidine, penicillamine, antiretrovirals, neuroleptics (Rabbitt *et al.,* 2016)

Management of cramp symptoms

A range of approaches have been documented in the literature. These loosely fall into pharmacological and non-pharmacological management approaches. A selection of drugs used in the pharma approach are listed in Table 2.

Table 2: Pharma management of cramp symptoms

Medicinal product	**Effectiveness**
Quinine	Various evidence of varying quality describes some positive outcomes from quinine use. El-Tawil *et al*., undertook a Cochrane review involving 23 randomised controlled trials (RCT) using quinine. A total of 1500 participants were included in the trial. When compared to placebo, use of quinine reduced the number of episodes of cramp by 28% during a period of two weeks (El-Tawil *et al.,* 2015). Although quinine has been used by many cramp sufferers there are some serious side effects associated with its use. Reduction in the excitability of the motor end plate to nerve stimulation
Diltiazem	Data from RCT
Vitamin B complex	Data from RCT
Naftidrofuryl	Data from RCT
Orphenidrine citrate	Data from RCT
Magnesium	Data from RCT. May have a small positive effect in women during pregnancy
Verapamil	Data from open-label studies
Gabapentin	Data from open-label studies
Vitamin K2	Data from open-label studies
Menaquinone-7	Data from open-label studies
Baclofen	No supporting studies
Carbamezepine	No supporting studies
Phenytoin	No supporting studies

Adverse reactions reported by patients using quinine

Although quinine is probably the most widely recognised drug used in the management of cramp, it is not without concerns. A range of systems can be adversely affected by quinine and reported symptoms have included thrombocytopaenia, haemolytic anaemia, photosensitive eczema, lichen planus, interstitial nephritis, acute

kidney failure, pulmonary oedema, and hypotension (Rabbitt *et al.,* 2016). Other complications of quinine can be dose-related.

Non-pharma management

Many patients report they can manage the onset of an attack of cramp by stretching the muscles affected. In some cases, forcibly moving the foot into dorsi-flexion can relieve cramp in the calf muscles. The use of prophylactic stretching has been examined in some trials. These studies with small sample sizes have suffered from some methodological issues, *e.g.* providing adequate training for affected patients in how to carry out the stretching process, and the findings have been equivocal at best. Further studies with greater patient numbers and more attention to the delivery of the intervention would be beneficial.

In a Cochrane review in 2012, Blyton *et al.,* examined other non-pharma interventions to help cramp symptoms. These included: changes to footwear; taking horse chestnut seed extract; using night splints: avoiding heavy covers on the bed, and making changes to sleeping position. As in previous studies, the review by Blyton *et al.* focused mainly on studies involving calf stretching but found the evidence to be inconclusive due to the small number of trials suitable for inclusion in their review (Blyton *et al.,* 2012). Since the Blyton review, a small number of other trials have been undertaken and these show promising results, although need larger sample sizes to confirm their initial findings. Hallegraeff *et al.* identified that nightly stretching before going to sleep reduces the frequency and severity of nocturnal leg cramps in older adults (Hallegraeff *et al.*, 2012; Behringer *et al.,* 2014)

Further reading and information

Despite cramp being such a common symptom, there is surprisingly little available information concerning the non-pharma management of symptoms for patients who may be unable to use pharmacological management. Clear messages for practice include:

- Awareness of the comorbidities associated with cramp.
- Awareness of medications that can cause cramp and referral back to the patient's GP for review if appropriate.
- If describing calf-stretching exercises to patients, ensuring they are thoroughly explained to support compliance.

This article is a very brief summary and further more extensive information can be found in the Clinical Knowledge Summary for cramp which explores its symptoms, examination and management in greater detail.

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