Criteria in diagnosing nocturnal leg cramps: a systematic review

Joannes Hallegraeff1,2*, Mathieu de Greef1,3, Wim Krijnen1,3 and Cees van der Schans1,3

Abstract

Background: Up to 33% of the general population over 50 years of age are affected by nocturnal leg cramps. Currently there are no generally accepted clinical characteristics, which identify nocturnal leg cramps. This study aims to identify these clinical characteristics and to differentiate between them and the characteristics of restless leg syndrome and periodic limb disorder.

Method: A systematic literature study was executed from December 2015 to May 2016. This study comprised of a systematic literature review of randomized clinical trials, observational studies on nocturnal and rest cramps of legs and other muscles, and other systematic and narrative reviews. Two researchers independently extracted literature data and analyzed this using a standardized reviewing protocol. Modified versions of the Cochrane Collaboration tools assessed the risk of bias. A Delphi study was conducted to assess agreement on the characteristics of nocturnal leg cramps.

Results: After systematic and manual searches, eight randomized trials and ten observational studies were included. On the basis of these we identified seven diagnostic characteristics of nocturnal leg cramps: intense pain, period of duration from seconds to maximum 10 minutes, location in calf or foot, location seldom in thigh or hamstrings, persistent subsequent pain, sleep disruption and distress.

Conclusion: The seven above characteristics will enhance recognition of the condition, and help clinicians make a clear distinction between NLC and other sleep-related musculoskeletal disorder among older adults.

Keywords: Cramps, Nocturnal, Diagnosis, Aged, Sleep-wake transition disorder, Restless legs syndrome

Background

Nocturnal Leg Cramps (NLC) is a musculoskeletal disorder characterized by suddenly occurring, episodic, persistently painful, involuntary contractions of the calf, hamstrings or foot muscles at night [1]. Up to 33% of the general population over 50 years of age have complaints related to NLC [2]. In 20% of these cases, cramps also occur during rest periods in the daytime [3]. Sleep disturbances, which may seriously affect well-being and quality of life, are common among patients with NLC [4, 5]. Symptoms, as well as prevalence and incidence, progress with advancing age [1, 6]. There is no consensus about aetiology of NLC, however it is suggested that shortened muscle length among older less physically active people is a risk factor [1]. Medical pathologies associated with NLC are chronic liver and renal failure (haemodialysis), vascular diseases, magnesium or calcium deficiency, dehydration and varicose veins [2, 7]. A pre-stretching protocol by physical therapists, as well as medical treatment blocking the medial branch of the deep peroneal nerve after lumbar surgery, may be effective in treating NLC [8, 9].

In contrast to the restless leg syndrome (RLS) and the idiopathic periodic limb movement disorder (PLMD), diagnosing NLC is hindered due to lack of a categorical definition of NLC. Moreover, different types of muscular cramps such as idiopathic, rest, leg, or pregnancy-related cramps are similar to NLC symptoms and are often confused in the literature [10].

Diagnostic criteria for RLS are clearly stated as follows: uncomfortable and unpleasant sensations in the legs, feet or arms associated with an urge to move; relief of symptoms by moving the affected limb; occurrence during rest in the evening or at night [11, 12]. The International
Restless Leg Syndrome Study Group approved the validity of a rating scale for RLS, which reflects the severity of the discomfort [11]. Idiopathic PLMD symptoms include the repetitive jerking movements of the leg for approximately 20-30 seconds during sleep, with the complaints when awake being more intense than during sleep. PLMD can be classified into mild, moderate, and severe levels as measured by the Periodic Limb Movement Index. Additionally, both RLS and PLMD may co-exist [12]. No consensus has been reached regarding the diagnostic criteria for NLC, or how to differentiate them from the RLS and PLMD criteria [12]. Primarily based on the patient history, the diagnosis of NLC may be confused with RLS or PLMD [1].

Generally, nocturnal pain can be a symptom of a serious pathology such as Parkinson disease, cardiovascular and renal diseases, lumbar canal stenosis, ostearthritis, peripheral neuropathy or cirrhosis. It is important to differentially diagnose NLC when is present as a nonspecific musculoskeletal disorder, or related to serious pathology.

This study focuses on strengthening the available criteria in order to prevent the misdiagnosis of NLC, for RLS or PLMD. The first aim of this literature review is to identify characteristics for diagnosing NLC. The second aim is to differentiate these diagnostic characteristics from other sleep-related disorders, such as RLS and PLMD, for application in clinical care.

**Method**

A systematic review was done to identify diagnostic criteria of NLC. The methodology is specified in our PROSPERO-registered protocol (16467) and conforms to Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guidelines [13]. In order to differentiate between NLC, on the one hand, and RLS and PLMD, on the other, an additional Delphi methodology was used. In this study a focus group of 27 experts assessed the relevance of the diagnostic criteria.

**Sourcing information**

An experienced librarian assisted in the development of a search strategy to identify recognized terminology. Four electronic databases were used including MEDLINE, Cinhahl, EMBASE and PEDro (1990 to May 2016).

The search included all commonly used terms for NLC such as ‘cramps’, ‘muscle cramps’, ‘nocturnal leg cramps’, ‘leg cramps’, ‘night leg cramps’, ‘rest cramps’, ‘sleep-wake transition disorders/classification’, ‘aged’, ‘aging’, ‘elderly’, ‘senior’, ‘diagnosis’, ‘classification’, ‘epidemiology’, ‘rehabilitation’, ‘parasomnias’, ‘clinical trial’, ‘randomized controlled trial’, ‘observational study’, ‘clinical study’, ‘systematic review’, ‘meta-analysis’, ‘validation study’ or ‘letter’.

**Selection criteria**

Inclusion criteria included randomised clinical trials, or observational studies reflecting NLC, muscle cramp, leg cramp, or rest cramp. The studies had to use the diagnostic criteria and classification in older adults aged over 50 years. A time frame spanning the previous 25 years.

Studies with non-English abstracts were excluded.

Two authors (JMH and MHGdG) independently extracted, screened, and reviewed all titles and abstracts of the retrieved articles. The articles were interpreted and classified into randomised clinical trials and observational studies. Reference lists of any recent reviews were hand searched in order to identify additional studies and help in excluding any duplicates.

**Data extraction**

The characteristics, diagnostic features and population characteristics of the investigated populations were summarised and catalogued. Randomised clinical trials and observational studies were screened for descriptions of diagnostic terms or classification criteria for NLC during sleep among adults aged over 50. For each included study, descriptive data regarding the participants and diagnostic terms were extracted. A flowchart was made to show the process of the literature search [13].

**Quality assessment**

Cochrane checklists for randomised clinical trials and observational studies were appraised using the methodological quality (risk of bias) of the included studies. To discuss any discrepancies between the two reviewers, consensus meetings were arranged. Complete agreement was reached after discussions with a third reviewer (CvdS) in all of the cases.

**Delphi sub-study**

The Delphi methodology was performed to examine the relevance of the extracted diagnostic criteria found in the systematic review. A questionnaire with closed-ended questions on a five-point Likert scale (always – mostly – sometimes – never - not known) was presented to a focus group of experts. The questionnaire was developed based on the results of the literature search and comprised the following items: (1) Are you known with NLC; (2) NLC has a sudden onset; (3) NLC is only present at night; (4) Pain and/or intense pain is the main characteristic; (5) NLC duration varies from seconds to 10 minutes; (6) NLC location is thigh, calf or foot; (7) After reduction of NLC there will be pain afterwards; (8) NLC might be associated with sleep disruption; (9) NLC is associated with medication use / comorbidity; (10) NLC might be associated with distress. The designated criteria for inclusion were established by more than 50%
of the respondents. Geriatric experts were randomly chosen on the basis of their expertise in geriatric health.

**Results**

After completing the systematic search and manual searches of the reference lists of the systematic reviews and narrative reviews and after removing duplicates and records not meeting the inclusion criteria, in the screening a total of 221 papers were yielded of which 162 were irrelevant and had to be excluded due to not meeting titles and abstracts. This resulted in 59 records that were appropriate for further evaluation. Subsequently, 41 full-text articles were excluded because they did not describe diagnostic criteria of NLC in older adults. No primary studies with the focus on diagnosing were found. Eight randomised clinical trials and ten observational studies were eligible for analysing classification characteristics of NLC. Full consensus between MHG and WPK was reached regarding the included citations. Figure 1 presents the selection of the studies through the review process.

Two randomised clinical trials [14, 15] had high and unclear risk of bias due to a lack of internal validity, however the description of the included NLC patients was adequate.

The groups were treated equally in all studies, and the randomisation procedure was performed well, except in one instance. Among the observational studies two showed low risk of bias [4, 16]. In all studies, the populations were well defined.

See Tables 1 and 2 for risk of bias and Table 3 for the description of the study characteristics.

The total number of participants in the 18 included studies was 36,515 of which the study of Garrison et al. 2015 included 31,339 participants. Overall, 51% of the participants were male and mean age of participants was 64 years (range 51-75 years).

Comorbidities were categorized in five domains:
Heart and vascular diseases: coronary artery disease, peripheral vascular disease, hypertension, varicose veins, ankle oedema, vascular occlusive disease and leg claudication.

Kidney diseases: renal dialysis, haemodialysis, uraemia, hypocalcaemia and hypokalaemia.

Neurological diseases: neuropathies, motor neuron disease, radiculopathy or hereditary cramp syndromes, neuromuscular or neurological diseases, peripheral neuropathy, Amyotrophic Lateral Sclerosis, poliomyelitis, lumbar spinal radiculopathy, lumbar canal stenosis and stroke.

Musculoskeletal disorders: arthritis and myopathies.

Metabolic disorders: Diabetes Mellitus, plasma electrolyte abnormalities hepatic, liver cirrhosis, postphlebitic syndrome volume depletion.

---

### Table 1 Risk of bias of the included randomised clinical trials (9-item Cochrane checklists for randomised trials)

| Study            | Randomisation | Concealed randomization | Blinded patients | Blinded treaters | Blinded Assessors | Groups comparable | Loss to follow up | Intention to treat | Groups treated equally |
|------------------|---------------|-------------------------|------------------|------------------|-------------------|------------------|------------------|-------------------|----------------------|
| Connolly 1992    | +             | -                       | +                | +                | -                 | +                | -                | -                 | +                    |
| Coppin 2005      | +             | +                       | -                | +                | +                 | +                | +                | +                 | +                    |
| Garrison 2011    | +             | +                       | +                | +                | +                 | +                | +                | +                 | +                    |
| Hallegraeff 2012 | +             | +                       | +                | +                | +                 | +                | +                | +                 | +                    |
| Jansen 1997      | +             | +                       | +                | +                | +                 | +                | +                | +                 | +                    |
| Roffe 2002       | +             | +                       | +                | +                | -                 | +                | +                | +                 | +                    |
| Serrao 2001      | -             | -                       | -                | -                | -                 | -                | +                | -                 | +                    |
| Young 1993       | -             | -                       | ?                | ?                | ?                 | ?                | -                | ?                 | +                    |

Connolly 1992 [29], Coppin 2005 [5], Garrison 2011 [17], Hallegraeff 2012 [9], Jansen 1997 [18] and Roffe 2002 [19] showed low risk of bias.

### Table 2 Risk of bias of the included observational studies (9-item Cochrane checklist for observational studies)

| Study          | Groups well defined | Selection bias | Exposure | Outcome | Blinding | Follow-up | Loss to follow up | Confounding | Generalizability |
|----------------|---------------------|----------------|----------|---------|----------|-----------|-------------------|-------------|------------------|
| Angeli 1996    | +                   | -              | +        | +       | -        | +         | -                 | +           | +                |
| Baskol 2004    | +                   | +              | +        | +       | -        | ?         | ?                 | +           | +                |
| Garrison 2015  | +                   | +              | +        | +       | +        | +         | +                 | +           | +                |
| Garrison 2012  | +                   | -              | -        | +       | +        | +         | -                 | +           | +                |
| Hawke 2013     | +                   | +              | +        | +       | +        | +         | +                 | +           | +                |
| Hawke 2013     | +                   | +              | +        | +       | +        | +         | +                 | +           | +                |
| Hirai 2000     | +                   | -              | +        | +       | +        | -         | ?                 | -           | +                |
| Naylor 1994    | +                   | +              | +        | -       | +        | ?         | ?                 | ?           | +                |
| Nishant 2014   | +                   | -              | +        | +       | -        | +         | -                 | -           | +                |
| Oboler 1991    | +                   | -              | +        | +       | +        | -         | ?                 | ?           | -                |

Baskol 2004 [21], Garrison 2015 [22], Hawke 2013 [4] and Hawke 2013 [24] showed low risk of bias.
| Table 3 Characteristics of the included studies |
|-----------------------------------------------|
| **Randomized clinical trials**                |
| Study objective                               | Diagnostic criteria                                                                 | Comorbidities associated with NLC and medication use |
| **Number of participants**                    |                                                                                     |                                                          |
| Age                                           | Nocturnal leg cramps. Aged > 50. At rest or sleep.                                    | Coronary artery disease, Peripheral vascular disease, |
| Male                                          | Foot, lower part of leg, sometimes thigh. Sleep interruption.                        | Hypertension, Diabetes Mellitus                         |
| Connolly 1993 [29]                            |                                                                                     | *Medication: diuretics*                                  |
| 6/9                                           |                                                                                     |                                                          |
| Efficacy of quinine                           | Nocturnal leg cramps, aged > 60, painful and involuntary. Muscle spasms. Disrupt    | Renal dialysis, asthma and hypertension.                |
|                                              | sleep. Disruption. Most commonly in the leg, relief by stretching.                   | *Medication: diuretics, nifedipine, salbutamol and      |
|                                              |                                                                                     | terbutaline                                               |
| COPPIN 2005 [5]                               |                                                                                     |                                                          |
| 8/9                                           |                                                                                     |                                                          |
| Effect of calf stretching                      |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Garrison 2011 [17]                            |                                                                                     | Participants with comorbidities excluded                |
| 9/9                                           |                                                                                     |                                                          |
| The effect of magnesium in individuals with leg cramps |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Hallegraeff 2012 [9]                          |                                                                                     |                                                          |
| 9/9                                           |                                                                                     |                                                          |
| Effect of pre sleep stretching                 |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Jansen 1997 [18]                              |                                                                                     |                                                          |
| 9/9                                           |                                                                                     |                                                          |
| Efficacy of hydro quinine in muscle cramps    |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Roffe 2002 [19]                               |                                                                                     |                                                          |
| 8/9                                           |                                                                                     |                                                          |
| The effect of magnesium in chronic non-pregnant individuals |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Serrao 2001 [14]                              |                                                                                     |                                                          |
| 3/9                                           |                                                                                     |                                                          |
| To evaluate the efficacy and safety of         |                                                                                     |                                                          |
| gabapentin in the treatment of muscle         |                                                                                     |                                                          |
| Cramps                                       |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Young 1993 [15]                               |                                                                                     |                                                          |
| 1/9                                           |                                                                                     |                                                          |
| The effect of naftidrofuryl in individuals    |                                                                                     |                                                          |
| with rest cramps                              |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Observational studies                         |                                                                                     |                                                          |
| Angeli 1996 [20]                              |                                                                                     |                                                          |
| To define the features, prevalence, and       |                                                                                     |                                                          |
| pathophysiology of therapy for muscle         |                                                                                     |                                                          |
| and small muscles cramps in cirrhotic patients.|                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Baskol 2004 [21]                              |                                                                                     |                                                          |
| 6/9                                           |                                                                                     |                                                          |
| The prevalence of muscle cramps in non-alcoholic cirrhosis patients. |                                                                                     |                                                          |
|                                              |                                                                                     |                                                          |
| Garrison 2015 [22]                            |                                                                                     |                                                          |
hyponatremia, hypothyroidism, hyper- and hypothyroidism and acute extracellular volume depletion including excessive perspiration.

The analysis of 18 primary studies revealed twelve different diagnostic criteria used: ‘rest, sleep or night’ \( (n = 16) \); ‘painful’ \( (n = 12) \); ‘aged > 50’ \( (n = 8) \); ‘involuntary’ \( (n = 10) \); ‘sudden onset’ \( (n = 7) \); ‘posterior calf, foot or thigh’ \( (n = 8) \); ‘sleep disruption’ \( (n = 7) \); ‘persisting pain afterwards’ \( (n = 4) \); ‘duration from seconds to several minutes’ \( (n = 5) \); ‘distress’ \( (n = 4) \); ‘stiffness’ \( (n = 1) \) and ‘asymmetrical cramps’ \( (n = 1) \) [4, 9, 14–27].

**Clinical classification characteristics**

After counting the number of times the criteria were described, and after comparing the twelve criteria to RLS

### Table 3 Characteristics of the included studies (Continued)

| Study               | Description                                                                 |
|---------------------|-----------------------------------------------------------------------------|
| Garrison 2012 [16]  | Evaluating the association between diuretics, statins and long-acting \( \beta_2 \) agonist’s use. |
| Hawke 2013 [4]     | Impact of NLC on health related quality of life.                            |
| Hawke 2013 [23]    | Factors associated with night-time calf muscle cramps                       |
| Hirai 2000 [24]    | NLC in general population and in patients with varicose veins               |
| Naylor 1994 [25]   | Prevalence, severity and correlation with vascular diseases                |
| Nishant 2014 [26]  | Prevalence of nocturnal leg cramps in LSCS patients and in general population. |
| Oboler 1991 [27]   | Prevalence and treatment regimens of NLC                                   |

In total 18 studies are included for analysing NLC characteristics: eight randomized clinical trials and ten observational studies.

---

Medication: diuretics and long-acting \( \beta_2 \) agonists

Participants with comorbidities known to cause cramp excluded

Hamstring tightness. Foot or leg coldness

Participants with comorbidities known to cause cramp were excluded

Varicose veins

Peripheral vascular disease

Amyotrophic lateral sclerosis, poliomyelitis, peripheral neuropathy, lumbar spinal radiculopathy; metabolic disorders including diabetes, pregnancy, uremia, liver cirrhosis, and hyper- and hypothyroidism; acute extracellular volume depletion including excessive perspiration, hemodialysis, diarrhea, and diuretic therapy; hereditary disorder. Hypertension, hypocalcaemia, hypokalaemia, vascular diseases.

Medications: diuretics, antidepressants, calcium blockers, statins, and steroid, nifedipine-blockers. Arthritis, Peripheral vascular disease, Hypokalaemia, Coronary artery disease, Hypertension, Kidney disease, Stroke, Diabetes Mellitus, Hypocalcaemia.
and PLMD criteria, the following criteria were deemed not distinctive enough: ‘at rest or sleep,’ ‘aged,’ ‘involuntary,’ ‘sudden onset,’ ‘stiffness’ and ‘asymmetrical.’ As a result, the following seven criteria remained in order to differentiate NLC from RLS and PLMD: ‘pain,’ ‘intense pain,’ ‘period of seconds to a maximum of 10 minutes,’ ‘located in posterior calf or foot,’ ‘subsequent pain,’ ‘sleep disruption’ and ‘distress.’ These seven classification characteristics differentiate from RLS and PLMD. See Table 4.

Discussion
This review has identified seven criteria, derived from consensus, which can be employed as a framework to differentiate NLC from RLS or PLMD. Distress and sleep disruption are indicated in a limited number of studies and are associated with negative impacts on physically related aspects of the quality of life [4]. Similarly, ‘subsequent pain’ is also a criterion as a consequence of the occurrence of NLC. The NLC characteristics that were revealed as the most discriminatory – compared to those of RLS and PLMD – include intense pain with duration of a maximum of ten minutes in the calf or the foot, with relief of the symptoms occurring with no intervention. In contrast to NLC, pain in rest or during sleep in the calf or foot can also be due to vascular insufficiency.

In contrast to previous studies, that included all kind of cramps in different ages, the current review focused on NLC among older adults aging 50 years and older therefore excludes other types of cramps [1–3, 28]. Naylor et al. 1994, showed the highest prevalence of NLC is in age group 60-69 years, which is in line with our result with a mean age of the total population in the included studies of 64 years [25]. We also confirmed the previous findings that vascular and renal comorbidities are the most stated and are clinically relevant in elderly people [4, 9, 19–21, 25, 27, 29]. In addition, the use of diuretics is known to cause muscle cramps [9, 16, 21, 24–26, 29]. Consequently, we suggest that vascular and renal comorbidities as well as the use of diuretics could be considered as correlational factors for NLC. This may improve the accuracy of future NLC diagnoses.

Managing the symptoms of patients with NLC can be a challenge in daily clinical practice considering how recent some developments in the diagnosis and treatment

| Table 4 | Involuntary musculoskeletal disorders at rest or nocturnal with sudden onset in elderly above 50 |
|---------|------------------------------------------------------------------------------------------------|
|         | Nocturnal leg cramps | Restless leg syndrome | Periodic Limb Movement Disorder |
| Pain    | ✓                    |                      |                                |
| Intensely pain | ✓                    |                      |                                |
| From seconds to maximum 10 minutes | ✓                    |                      |                                |
| Calf or foot, seldom thigh | ✓                    |                      |                                |
| Persisting pain afterwards | ✓                    |                      |                                |
| Sleep disruption | ✓                    |                      |                                |
| Distress* | ✓                    |                      |                                |
| Irritating, burning, crawling sensations | ✓                    |                      |                                |
| In episodes | ✓                    |                      |                                |
| An urge to move | ✓                    |                      |                                |
| Reduction of symptoms by activity | ✓                    |                      |                                |
| No pain | ✓✓                   |                      |                                |
| Repeating and jerking movements | ✓                    |                      |                                |
| Duration 20-30 seconds | ✓                    |                      |                                |

Reduced strength of dorsiflexion of ankle, foot and toes was also found in one study and can be associated with NLC [23]. The response rate of the geriatric clinicians in the focus group of the Delphi study was 52%, all with > 50% consensus. See Table 5

| Table 5 | Delphi study items |
|---------|--------------------|
|         | Always | Mostly | Sometimes | Never | Not known |
| Are you known with NLC | 30*  | 40 | 20 | 0 | 10** |
| • NLC has a sudden onset | 33 | 56 | 11 | 0 | 0 |
| NLC is only present at night | 11 | 68 | 11 | 0 | 11 |
| • Pain and / or intense pain is the main characteristic | 10 | 80 | 0 | 0 | 10 |
| NLC duration varies from seconds to 10 minutes | 10 | 80 | 0 | 0 | 10 |
| NLC location is thigh, calf or foot | 33 | 45 | 11 | 0 | 11 |
| • After reduction of NLC there will be pain afterwards | 0 | 50 | 40 | 0 | 10 |
| NLC might be associated with sleep disruption | 10 | 50 | 20 | 0 | 20 |
| NLC is associated with medication use / comorbidity | 0 | 11 | 67 | 0 | 22 |
| • NLC might be associated with distress | 10 | 10 | 60 | 10 | 10 |

Seven criteria differentiating NLC from RLS and PLMD. *Percentages; ** if ‘no’ excluded from these survey (n = 3)
of the disorder are. Therefore, we suggest that these developments indicate extending the scope of clinical care. The framework introduced in this review provides a natural guide to future research within the population of older adults with musculoskeletal disorders during rest or sleep. Further research on the reliability and validation of the proposed theoretical framework is necessary for clinical application and diagnostic accuracy.

In addition, two clinical test procedures were reported for diagnostic application: the forceful knee flexion test indicated findings of cramps; the examiner applies a force to overcome knee flexion when testing in a prone position. Most patients with lumbar disc herniation comorbid with leg cramps also showed positive findings during this test, and cramps could be induced \( (n = 2) \) [26, 30]. There is a need for diagnostic studies in regard to these clinical tests on NLC and it will be interesting to assess their benefits as well [26, 30].

A potential limitation of this review is the lack of primary studies with the focus on diagnosing NLC in older adults. Therefore, as much as possible, the risk of bias was limited by using clearly defined inclusion criteria and conducting a thorough screening and reviewing process of the presented literature. Inherent in this process was the inclusion of patients with several comorbidities in the separate studies. Although these comorbidities might have influenced the interpretation of NLC, it does reflect the clinical relevance of patients with this disorder.

Conclusions

An extensive history taking including the above seven characteristics may rule out other disorders in diagnosing idiopathic NLC. In conclusion, seven relevant clinical characteristics have been identified to diagnose patients with NLC, and specifically differentiate this disorder from RLS and PLMD. These characteristics enhance the recognition and diagnosis of this highly prevalent, musculoskeletal sleep-related disorder.

Abbreviations

NLC: Nocturnal leg cramps; PLMD: Periodic limb movement disorder; RLS: Restless leg syndrome

Acknowledgements

The content is solely the responsibility of the authors, who have all made substantial contributions to the study’s conception and design, and the analysis and interpretation of the data, the draft and revision of the article and the final approval of the version to be submitted. Mrs A. Hartman of the University library optimized the search strategy. Also thanks to Mrs A. White and Mr D. White who edited the manuscript and improved English expression.

Funding

This project did not receive any funding.
16. Garrison SR, Dormuth CR, Morrow RL, Carney GA, Khan KM. Nocturnal leg cramps and prescription use that precedes them: a sequence symmetry analysis. Arch Intern Med. 2012;172:120–6.

17. Garrison SR, Birmingham CL, Koehler BE, McCollom RA, Khan KM. The effect of magnesium infusion on rest cramps: randomized controlled trial. J Gerontol A Biol Sci Med Sci. 2011;66:651–6.

18. Jansen PH, Veenhuizen KC, Wesseling AI, de Boor T, Verbeeck AL. Randomised controlled trial of hydroquinine in muscle cramps. Lancet. 1997;349:528–32.

19. Roffe C, Sills S, Crome P, Jones P. Randomised, cross-over, placebo controlled trial of magnesium citrate in the treatment of chronic persistent leg cramps. Med Sci Monit. 2002;8:326–30.

20. Angell P, Albino G, Carraro P, Dalla Pria M, Merkel C, et al. Cirrhosis and muscle cramps: evidence of a causal relationship. Hepatology. 1996;23:264–73.

21. Baskol M, Ozbakir O, Coskun R, Baskol G, Saraymen R, et al. The role of serum zinc and other factors on the prevalence of muscle cramps in non-alcoholic cirrhotic patients. J Clin Gastroenterol. 2004;38:524–9.

22. Garrison SR, Dormuth CR, Morrow RL, Carney GA, Khan KM. Seasonal effects on the occurrence of nocturnal leg cramps: a prospective cohort study. CMAJ. 2015;3(187):248–53.

23. Hawke F, Chuter V, Burns J. Factors associated with night-time calf muscle cramps: a case-control study. Muscle Nerve. 2013;47:339–43.

24. Hirai M. Prevalence and characteristics of muscle cramps in patients with varicose veins. Vasa. 2000;4:269–73.

25. Naylor JR, Young JB. A general population survey of rest cramps. Age Ageing. 1994;5:418–20.

26. Nishant, Chhabra HS, Kapoor KS. Nocturnal cramps in patients with lumbar spinal canal stenosis treated conservatively: a prospective study. Asian Spine J. 2014;8:624–31.

27. Oboler SK, Prochazka AV, Meyer TJ. Leg symptoms in outpatient veterans. West J Med. 1991;155:256–9.

28. Rana AQ, Khan F, Mosabbir A, Ondo W. Differentiating nocturnal leg cramps and restless legs syndrome. Expert Rev Neurother. 2014;14:813–8.

29. Connolly PS, Shirley EA, Wasson JH, Nierenberg DW. Treatment of nocturnal leg cramps. A crossover trial of quinine vs vitamin E. Arch Intern Med. 1992;152:877–80.

30. Demircan MN, Colak A, Kuflay M, Kibici K, Topuz K. Cramp finding: can it be used as a new diagnostic and prognostic factor in lumbar disc surgery? Eur Spine J. 2002;11:47–51.