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LORENZO, Mathieu, et al.

Abstract

Background. Approximately one out of two individuals over the age of 60 suffers from nocturnal leg cramps. These often have an important impact on the person’s quality of life. Different drug and non-drug treatments are proposed to treat these cramps, but none to date have been shown to be both safe and effective. The objective of this study was to describe the drug and non-drug treatments used by primary care patients suffering from cramps.

Methods. We used data collected as part of two cross-sectional surveys of patients aged 60 years and older attending general practices in the French region of Alsace. We asked the participants suffering from cramps if they were currently using a treatment for their cramps. We distinguished potentially harmful from unharmful treatments.

Results. Overall, 632 patients suffering from cramps were included in our study. Only 133 patients (19.5%) were taking a treatment for cramps. 82 patients used one or several of 17 different drug treatments. 58 patients used one or several of 13 different types of non-drug treatments. Potentially harmful treatments, mostly Quinine made up 16.7% (n = [...])

Reference

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Treatment of nocturnal leg cramps by primary care patients over the age of 60

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Abstract

Background. Approximately one out of two individuals over the age of 60 suffers from nocturnal leg cramps. These often have an important impact on the person’s quality of life. Different drug and non-drug treatments are proposed to treat these cramps, but none to date have been shown to be both safe and effective. The objective of this study was to describe the drug and non-drug treatments used by primary care patients suffering from cramps.

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Results. Overall, 632 patients suffering from cramps were included in our study. Only 133 patients (19.5%) were taking a treatment for cramps. 82 patients used one or several of 17 different drug treatments. 58 patients used one or several of 13 different types of non-drug treatments. Potentially harmful treatments, mostly Quinine made up 16.7% (n = 25) of all treatments used for cramps.

Conclusions. This study sheds light on the great diversity of therapeutic practices for cramps in outpatient care. Many of the treatments reported by patients have not previously been described in the medical literature. We recommend GPs to ask their patients about the treatments they take for cramps in order to make sure that they are safe.

Key words: Family practice, idiopathic nocturnal cramps, muscle cramps, muscle cramps drug therapy, muscle cramps therapy, primary care.

Introduction

Cramps are involuntary, painful contractions of one or several muscles which last from a few seconds to a few minutes (1). Most cramps occur at rest and mainly at night (2). The classification of Parisi (3) distinguishes idiopathic cramps (that notably include nocturnal leg cramps), para-physiological cramps accompanying pregnancy or physical activity and symptomatic cramps specifically induced by a treatment or a pathology. After 60 years of age, about one out of two individuals suffers from cramps (4,5). Cramps entail a change in quality of life primarily related to a change in the quality of sleep (6).

The muscle contractions at the origin of cramps are provoked by repetitive discharges of motor units extending gradually to a constant number of muscle fibres within a same muscle. The phenomenon responsible for the discharge emission seems to take place in the peripheral motoneuron (1,2).
The management of cramps includes advice on lifestyle and non-drug treatments (7). The latter include stretching exercises (8), elevation of the legs or massage of the lower limbs (9). However, the available evidence in relation to stretching exercises is contradictory and there has been little or no evaluation of the other methods (9–11). In 2012, a general population observational study, 24 different non-drug treatment had already been used at least once by more than 95% of participants to prevent cramp or reduce pain (12). They were mostly rated as being ‘useless’ or ‘a little help’ (12). Therefore, at present, the effectiveness of non-drug treatments for cramps remains uncertain (9,13).

Different drug treatments exist to manage cramps. Quinine has been shown to reduce the number, the frequency and the intensity of cramps with a good level of evidence (14). However, quinine can have serious side effects (such as cardiac arrhythmias and serious immuno-allergic reactions for example) (14). The risk/benefit ratio of quinine seems unfavourable and its prescription is no longer recommended in the treatment of cramps (13,14). Magnesium is often proposed but has not been shown to be effective to treat cramps (15). B-complex vitamins, certain sodium channel blockers, lidocaine or naftidrofuryl could have a modest effect on cramps, but the data comes from studies with a very low level of evidence (13). One study described that 18 different drug treatment had already been used at least once by more than 60% of participants to prevent cramp (12). All except quinine and magnesium were mostly rated as being ‘useless’ or ‘a little help’ (12). Therefore, at present, no drug treatment for cramps has been shown to be both effective and without danger.

In summary, in order to treat cramps, the drug and non-drug treatment options are overabundant, without any particular strategy being favoured. To our knowledge, there is no data on patients’ current use of different drug or non-drug treatments. It would however be interesting to confront the limits of the treatment options with the reality of their use in clinical practice.

Objective

The objective of this study was to describe the drug and non-drug treatments currently used by patients, suffering from cramps in primary care.

Methods

Design

We did a secondary analysis of the data gathered from two cross-sectional studies of patients aged 60 years and older attending primary care. These studies were carried-out within the Strasbourg General Medicine Department Practice Based Research Network (GMDPBRN). During 6 months in 2011, the CIPAprev study, explored the prevalence of cramps (5). During 7 months in 2012–2013, the CIPAsed study explored the links between cramps and a sedentary lifestyle (16).

Data collection

Data collection took place in 79 medical practices spread across the Alsace region. They were all members of the GMDPBRN. Among these, 21 practices participated in CIPAprev, 67 in CIPAsed. Twelve practices participated in both studies. Patients were prospectively sampled by the GPs using a systematic steps of 1 in 4 attending patients aged ≥60 years. Anonymized clinical data were collected by the GPs using a screening questionnaire during the consultation and were recorded into an electronic database in both studies. No patient could participate in both studies.

Participants

Participants were required to be 60 years old or older, autonomous in going about their daily life and going to see their general practitioner (GP) spontaneously for any reason. As the pathophysiological mechanism of exercise cramps is different, we did not consider individuals with cramps occurring only after or during exercise. The age limit of 60 was fixed based on the results of Naylor’s study which showed that patients between 50 and 59 years of age were less susceptible to suffer from cramps (6).

To evaluate whether our total sample was representative of the population of patients ≥60 years attending general practices in Alsace, we compared it to a population of patients aged between 60 and 90 years registered between October 2011 and March 2012 in the regional health insurance database.

Study population

Participating GPs proposed CIPAprev to 549 patients and CIPAsed to 1464 patients. 516 patients were included in CIPAprev (participation rate (PR)=94%) and 849 in CIPAsed (PR=54%). Among the 1365 study participants, 632 (239 in CIPAprev and 393 in CIPAsed) were experiencing cramps and were thus eligible for this analysis. The populations from the two studies were comparable for age, sex, number of cramps per month, and most comorbidities. The two populations differed for the mean number of treatments taken for other indications than cramps (3.3 vs 4.4 treatments (P < 0.01).

In both studies data collection was undertaken after informed consent, and all the patients who agreed to participate responded to the questionnaire. The difference in participation rate could be explained by the difference in study design. In CIPAprev, the data were collected in 15 minutes during the consultation time, while data collection in CIPAsed required several hours after the consultation time with the help of a research assistant.

Main outcome measures

Based on previously published reviews (4,6,7) and using a group-based iterative approach, we developed a 9 items screening questionnaire (5). The questions focused on demographics, the number of cramps per month and the patient’s medical history, and treatment. The questionnaire was pretested by eight GPs in three primary care practices to identify any source of difficulties or misunderstandings. The same questionnaire was used in the two studies.

The questionnaire was explicit in defining cramps as a painful involuntary muscle contraction when resting, lasting from a few seconds to a few minutes. We followed Parisi’s choice of Layzer’s clinical definition: ‘spasmodic, painful, involuntary, contraction of the skeletal muscle’, or in non-medical language: ‘sudden, involuntary and painful muscular contraction’ (2). This definition seems to be accepted by most of the authors (3,4,6,7,11,17). If in doubt as to whether the patient truly had cramps, GPs were advised to explore another typical feature i.e. whether stretching and contracting the antagonist muscle speeds up relief (17).

We asked the participants if they were currently using a treatment for their cramps, without specifying whether it was to relieve pain or prevent cramps. Examples of questions asked during the interviews are: ‘Currently, do you use any kind of treatment for your cramps’ ‘Are you taking something or doing something when you have cramps’. We used international non-proprietary names to
describe drug treatments. We used open-ended questions to make patients describe non-drug treatments and accepted up to 4 drug treatments and 3 non-drug treatments. The details of the non-drug treatments were not recorded verbatim, but entered in a summarized way into the electronic database.

We defined quinin, naftidrofuryl, levetiracetam, baclofen, carbamazepine and oxcarbazepine as potentially harmful treatments according to reported serious adverse events for cramps’ drug treatments (13). No non-drug treatments were considered potentially harmful (9).

Statistical analysis

The populations of patients suffering from cramps in the two studies were pooled for the analysis. We distributed the patients into two groups: group A for patients who used a treatment for their cramps, and group B for those who did not use treatments for their cramps. Data about the two groups were summarised using proportions and 95% confidence intervals. We compared the two groups for age, sex, number of cramps per month, medical conditions and number of treatments taken for another indication than cramps using chi-square tests or Fisher non-parametric tests for proportions.

We carried out a multivariate logistic regression for data with \( P < 0.20 \) in univariate analyses in the two groups. Backward stepwise variable selection on using a treatment for cramps was performed until no further variables could be deleted without a statistically significant loss of fit. The final model was the model containing only factors significantly associated with the dependent variable.

Group A was further split into three further categories: (i) patients who used both drug and non-drug treatments, (ii) those who only used drug treatments, and (iii) those who only used non-drug-treatments.

In these three categories, we described (i) the number of treatments used and (ii) the number and proportion of patients using a potentially harmful treatment. We computed means and 95% confidence intervals and compared quantitative data in univariate analyses using Student \( t \)-test or Mann–Whitney \( U \) test.

Age group and sex distributions in our sample were compared with the general population using chi-square tests with continuity corrections.

All statistical tests were two-tailed. A \( P \) value <0.05 was considered statistically significant.

All analyses were performed using R software, version 3.0 (18).

Results

We included 632 patients suffering from nocturnal leg cramps, 239 patients came from the first study and 393 from the second. The mean age was 70.5 ± 7.2 years of age. Three hundred and fifty-seven participants (56.5%, [95% CI = 51.2–61.8]) were female. The study population was comparable to the reference population concerning the breakdown by gender (\( P = 0.99 \)). Our study population varied slightly from the reference population with regard to four age groups (Supplementary Material).

Patients were suffering from a mean of 3.4 ± 2.9 episodes of cramps per month. They were using a mean of 3.7 ± 2.4 drug treatments for indications other than cramps. Four hundred and twenty-six patients (67.4% [95% CI = 63.8–71.0]) were suffering from high blood pressure, 104 (16.5% [95% CI = 13.6–19.3]) from diabetes, 91 (14.4% [95% CI = 11.7–17.1]) from venous insufficiency, 67 (10.6% [95% CI = 8.2–13.0]) from peripheral arteriopathy, 25 (3.9% [95% CI = 2.4–5.5]) from restless leg syndrome.

Nearly 1 in 5 patients was using a treatment for cramps (\( n = 123, 19.5\% \) [95% CI = 12.1–26.9]). Among the patients taking a treatment for cramps, about half were taking a drug treatment only (\( n = 65, 52.8\% \) [95% CI = 39.9–65.7]), a third only a non-drug treatment (\( n = 41, 33.3\% \) [95% CI = 17.7–48.9]), and the rest both a drug and non-drug treatments (\( n = 17, 13.8\% \) [95% CI = 0–33.1]).

The characteristics of patients who used a treatment are detailed in Table 1.

In total, the participants used 30 different treatments to relieve them from their cramps. The details of the different treatments are presented in Table 2.

Among the 632 patients, 82 (12.9% [95% CI = 5–20.8]) took at least one drug-treatment. Nearly one drug-treatment user in 3 used a potentially harmful treatment (\( n = 25, 29\% \)). These participants used 1.1 ± 0.3 drug treatments to treat their cramps. They reported 17 different drug treatments 5 of which were potentially harmful. The most common treatments were magnesium (\( n = 26 \)), quinine (\( n = 20 \)) and homeopathy (\( n = 16 \)). The potentially harmful treatment were Quinine (\( n = 20 \)), potassium (\( n = 2 \)), clonazepam (\( n = 1 \)), pregabalin (\( n = 1 \)) and amitryptilin (\( n = 1 \)).

Among the 632 patients, 58 (9.1% [95% CI = 0.8–17.4]) used at least one kind of non-drug treatment. These participants used 1.1 ± 0.4 different non-drug treatments to treat their cramps. They reported 13 different non-drug treatments. The most common were placebo soap in the bed (\( n = 18 \)), stretching (\( n = 11 \)) and applying heat or cold to the lower limbs (\( n = 9 \)).

Groups A (patients using a treatment for their cramps) and B (not using a treatment) were comparable for age, the number of cramps per month, the number of drug treatments for any indication other than cramps, and most medical conditions. In the treatment group, females were slightly over-represented (65.0% vs 54.4% \( P < 0.01 \), as was the prevalence of peripheral arteriopathy (12.0% vs 4.9% \( P = 0.02 \)) and the prevalence of diabetes (21.9% vs 15.1% \( P = 0.08 \)). Multivariate analysis revealed that using a treatment for cramps was associated with having peripheral arteriopathy (\( P < 0.01 \)) or diabetes (\( P = 0.04 \)). There was no difference on the number of cramps per month between the total population, the patients with peripheral arteriopathy and the patients with diabetes.

### Table 1. Characteristics of patients using or not a treatment for their cramps in our population gathered from two cross-sectional studies of patients aged of 60 years and older attending primary care in 2011, 2012, 2013

<table>
<thead>
<tr>
<th>Number of patients</th>
<th>( n = 632/% ) [95% CI]</th>
<th>Female sex (% [95% CI])</th>
<th>Average age (minimum–maximum)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Not taking any treatment for cramps</td>
<td>509 (80.5% [77–84])</td>
<td>277 (54.4% [48–60])</td>
<td>70.4 (60–92)</td>
</tr>
<tr>
<td>Taking treatment for cramps</td>
<td>123 (19.5% [12,1–26,9])</td>
<td>80 (65% [53.9–76.1])</td>
<td>70.8 (60–88)</td>
</tr>
<tr>
<td>Drug treatments only</td>
<td>65 (52.8% [39.9–65.7])</td>
<td>40 (61.5% [45.2–77.8])</td>
<td>70.8 (60–88)</td>
</tr>
<tr>
<td>Non-drug treatments only</td>
<td>41 (33.3% [17.7–48.9])</td>
<td>26 (63.4% [43.0–83.8])</td>
<td>72 (60–87)</td>
</tr>
<tr>
<td>Both drug and non-drug treatments</td>
<td>17 (13.8% [0–33.1])</td>
<td>14 (82.3% [5.9–22.1])</td>
<td>67.9 (61–79)</td>
</tr>
</tbody>
</table>
Table 2. Frequency of different treatments used and proportion of patients taking them among those who used drug or non-drug treatments for cramps (n = 86)

<table>
<thead>
<tr>
<th>Drug treatments</th>
<th>n = 86 (% [95% CI])</th>
<th>Non-drug treatments</th>
<th>n = 64 (% [95% CI])</th>
</tr>
</thead>
<tbody>
<tr>
<td>Magnesium</td>
<td>26 (30.2% [10.6–49.8])</td>
<td>Putting soap in the bed</td>
<td>18 (28.1% [4.6–51.6])</td>
</tr>
<tr>
<td>Quinine</td>
<td>20 (23.2% [2.2–44.2])</td>
<td>Stretching exercises</td>
<td>11 (17.1% [0–43.9])</td>
</tr>
<tr>
<td>Homeopathy</td>
<td>16 (18.6% [0–40.8])</td>
<td>Thermal measures</td>
<td>9 (14.0% [0–42.2])</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>5 (5.8% [0–36.3])</td>
<td>Mobilisation of legs</td>
<td>7 (10.9% [0–41.1])</td>
</tr>
<tr>
<td>Paracetamol</td>
<td>4 (4.6% [0–37.6])</td>
<td>Massage of legs</td>
<td>5 (7.8% [0–41.3])</td>
</tr>
<tr>
<td>Potassium</td>
<td>2 (2.3% [0–48.1])</td>
<td>Increasing hydration</td>
<td>3 (4.7% [0–45.3])</td>
</tr>
<tr>
<td>Extract of leeches*</td>
<td>2 (2.3% [0–48.1])</td>
<td>Anti-cramp teases</td>
<td>2 (3.1% [0–52.1])</td>
</tr>
<tr>
<td>Diosmin</td>
<td>2 (2.3% [0–48.1])</td>
<td>Anti-cramp mattress</td>
<td>2 (3.1% [0–52.1])</td>
</tr>
<tr>
<td>Clonazepam</td>
<td>1 (1.2% [0–72.5])</td>
<td>Hepar® mineral water</td>
<td>2 (3.1% [0–52.1])</td>
</tr>
<tr>
<td>Iron</td>
<td>1 (1.2% [0–72.5])</td>
<td>Eating chocolate</td>
<td>2 (3.1% [0–52.1])</td>
</tr>
<tr>
<td>Amitriptyline</td>
<td>1 (1.2% [0–72.5])</td>
<td>Elimination of cheese</td>
<td>1 (1.6% [0–76.2])</td>
</tr>
<tr>
<td>Mephenesin</td>
<td>1 (1.2% [0–72.5])</td>
<td>Eating honey</td>
<td>1 (1.6% [0–76.2])</td>
</tr>
<tr>
<td>Pregabalin</td>
<td>1 (1.2% [0–72.5])</td>
<td>Swimming</td>
<td>1 (1.6% [0–76.2])</td>
</tr>
<tr>
<td>Arnica</td>
<td>1 (1.2% [0–72.5])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sterol glycosides</td>
<td>1 (1.2% [0–72.5])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ginko biloba</td>
<td>1 (1.2% [0–72.5])</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lovemonthol veratrol</td>
<td>1 (1.2% [0–72.5])</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Extract of leeches are sold in pharmacy as drug treatment for vascular diseases.

Discussion

Summary of main findings

Only one in five patients over 60 years old used drug and/or non-drug treatments to relieve or prevent their cramps. The diversity of treatments they used, however, was extremely high, with participants reporting the use of 30 different types of treatments (17 drug treatments and 13 non-drug treatments). Twenty-five patients (16.7% of those using treatments) used treatments, mostly Quinine that were potentially harmful. Peripheral arteriopathy and diabetes were associated with the use of a treatment for cramps in univariate and multivariate analysis.

Synthesis and interpretation

Only a minority of patients in our study reported using treatments to relieve or prevent their cramps. This is in contrast with the study by Blyton et al., in which every participant reported having already used at least one treatment (12). Blyton et al. did not, however, provide data about current use. Some of the patients in our study may have taken a treatment in the past and stopped it. The poor perceived effectiveness of treatments described several studies supports this hypothesis (12,13,15).

A third of patients using a treatment reported using only non-drug treatments. None of these treatments were considered potentially harmful. Many of the non-drug treatments reported in our study (such as, for example, placing soap in the bed) had not previously been mentioned in the literature. Thermal measures (applying heat or cold), massages, moving the legs are commonly advised by physicians to treat cramps (7). These results are in line with those obtained by Blyton et al. in a general population study (12). Beyond leg stretching, the benefits of which can potentially be correlated to the pathophysiology of cramps (11), the use of some of the non-drug treatments found in our study seems to rest on folk explanations. For example, some believe the potassium contained in Marseille soap spreads through to the muscular cells in order to compensate for the potassium deficit responsible for the occurrence of cramps (19). As electrolyte imbalance is one of the proposed physiopathological theory to explain the occurrence of cramps (20), the effectiveness of this folk remedy may indeed deserve further exploration. In the end, all of these non-drug treatments present the benefit of preserving patients from serious adverse events or drug interactions associated with the use of drug treatments for cramps.

As expected common drug treatments such as magnesium and quinine were among those most commonly used by patients. Although quinine has been shown to reduce the number of cramps, its use is no longer recommended to treat or prevent cramps (14). There is currently no evidence that magnesium is truly effective in reducing cramp frequency in older patients (15). None of the other drugs described in the literature, such as the vitamin B complexes, certain inhibitors of calcium channel blockers, lidocaine and naftidrofuryl, were reported by the patients in our study (13). This suggests GPs in our study use a more limited spectrum of treatments than previously described in the literature. However, patients also used an important variety of drug treatments that had never been tested for effectiveness to prevent cramps. These findings are consistent with those of Blyton et al. and suggest that in the absence of effective and safe alternatives, patients may be inclined to choose a variety of over-the-counter options (12).

In our sample, the number of cramps per month was lower than in other studies (4,6). This result may be explained by differences in settings and population (5). As peripheral arteriopathy and diabetes were associated with the use of a treatment for cramps, these findings must be interpreted with caution. We found no previous studies in line with these findings. We hypothesize that it may have been difficult for the patient to distinguish pain associated with peripheral arteriopathy or diabetic neuropathies from pain associated with cramps, more frequently leading patients with these disorders to report having cramps.

Given the lack of evidence for any convincing treatment for muscle cramps (12,13), GPs should aim for safety. The potentially harmful therapies make up 16.7% of treatments used by patients for cramps. Questioning patients about the treatments they still use, and providing information about their safety could contribute to avoiding potentially serious adverse events.

Strengths and weaknesses

This study contributes new data on the diversity of treatment for cramps among primary care patients aged 60 years old or older.
Treatment of nocturnal leg cramps

at a regional scale. It sheds light on the reality of the management of cramps by placing the scientific data into perspective, by comparing it to the treatments used by patients in reality. Although slightly younger than the reference population, our population can be considered representative of patients older than 60 years old, who go to see their general practitioner in the region of Alsace.

However, this study remains an observational study, based on declarative data about current use. We did not enquire about previous treatments for cramps and thus are unable to completely compare our findings with those from previous studies.

Implication for practice and further research
The vast majority of patients suffering from cramps declared that they were not currently using any treatment to relieve their symptoms. However, studies on the quality of life showed that nearly half of the patients suffering from cramps, considered the discomfort they felt from cramps to be important or major (6,12). The reasons for which, despite this, patients refrain from treatment warrants further investigations. Further research is needed to identify effective drug and non-drug treatments for this extremely common disorder.

Conclusion
All in all, the variety of drug and non-drug treatments used by the patients illustrates the vagueness that surrounds the subject of cramps in primary care medicine: while the prevalence is known, the distribution of the frequency of cramps, their painful intensity, the expectations from treatments by patients and the effectiveness of treatments remain little explored. Within the uncertainty surrounding the best treatment for cramps, the safety of a potential treatment must be prioritised. From this point of view, our results are encouraging as in total 83% of the treatments to relieve cramps which were used by the patients in our study were not considered harmful.

Within the current context and development of knowledge in this field, it might be important for GPs to explore the treatments taken by patients for their cramps and to make sure they are safe. More research is needed to determine the effectiveness and the place of drug and non-drug treatments non-drug treatments in the prevention and management of idiopathic nocturnal leg cramps.

Supplementary Material
Supplementary data are available at Family Practice online.

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Declaration
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