Association Between Alcohol Consumption and Nocturnal Leg Cramps in Patients Over 60 Years Old: A Case-Control Study

Chloé Delacour, MD[1]

Juliette Chambe, MD[1]

François Lefebvre, MD[2]

Claire Bodot, MD[1]

Elodie Bigerel, MD[1]

Laetitia Epifani, MD[1]

Céline Granda, MD[1]

Dagmar M. Haller, MD, PhD[3]

Hubert Maisonneuve, MD[1,3]

[1]General Medicine Department, Faculty of Medicine, University of Strasbourg, Strasbourg, France

[2]Public Health Department, Faculty of Medicine, University of Strasbourg, Strasbourg, France

[3]Primary Care Unit, Faculty of Medicine, University of Geneva, Geneva, Switzerland

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CORRESPONDING AUTHOR

Chloé Delacour, MD
General Medicine Department,
Faculty of Medicine
University of Strasbourg, Strasbourg, France
4 rue Kirschleger
67000 Strasbourg France
chloe.delacour@unistra.fr

ABSTRACT

PURPOSE Nocturnal leg cramps are a specific kind of cramps affecting almost one-half of patients aged 60 years and older. They reduce patients' quality of sleep and have a negative impact on their quality of life. The aim of this study was to evaluate the association between nocturnal leg cramps and the consumption of alcoholic beverages in patients aged 60 years and older attending general practices.

METHODS Case-control study with a Bayesian approach for sensitivity analysis. Participants were voluntary ambulatory patients aged 60 years and older consulting their family doctor. They were recruited in 67 general practices across the Alsace region. Cases (patients having cramps), were matched with controls (patients free from cramps) for age, sex, medical history, and medications known to trigger cramps. Alcohol consumption was assessed through a standardized food frequency questionnaire.

RESULTS We found an association between the global consumption of alcoholic beverages and nocturnal leg cramps (OR = 6.5, 95% credibility interval, 1.68-38.05; posterior probability 99.82%).

CONCLUSION We identified an association between alcohol consumption and nocturnal leg cramps among patients aged 60 years and older attending general practices. These findings have implications for the prevention of cramps.

INTRODUCTION

The common definition of cramps is episodes of pain due to sudden, intense, and involuntary contractions of muscles lasting up to several minutes.[1,2] Resolution is either spontaneous or helped by stretching the contracted muscle.[3] Lower limbs are the first to be affected, especially the calf.[4,5] A specific kind of cramps occurring at night or during rest time has been identified as nocturnal leg cramps (NLC).[5-7]

The prevalence of NLC was studied in 2012 in a French population of patients aged 60 years and older.[8] Among this population, 46% reported NLC, 15% experienced cramps more than 3 times a month, and 31% were awakened by them.

Nocturnal leg cramps reduce quality of sleep and have a negative impact on physical aspects of health-related quality of life.[9] Nevertheless, patients rarely report their NLC symptoms to physicians and effective and safe treatments are lacking.[10-13]

Even though some specific medical conditions and drug treatments have been identified as causes of muscle cramps,[5,14] most cramps are considered idiopathic[6] and their exact pathophysiology remains unknown.[15-17] Thus far, there is a lack of observational studies, especially in primary care, focusing on lifestyle factors associated with NLC.[18,19] According to popular belief, the consumption of alcoholic beverages may cause mus-

cular stiffness. As far as we know, however, no studies have yet explored the association between alcohol consumption and NLC in elderly people.[20]

Our aim was to assess the association between NLC and the consumption of alcoholic beverages in elderly patients.

METHODS

Study Design

The study was conducted within the Strasbourg General Medicine Department practice-based research network. It was part of a larger study exploring the association between lifestyle and NLC.[21]

We carried out a case-control study in 2013. The study consisted of a 6-month screening phase which was followed by an 11-month data collection phase.

The STrengthening the Reporting of OBservational studies in Epidemiology (STROBE) statement was used to guide the reporting of the study. The study was approved by the Ethics Committee of the Mulhouse Hospital.

Study Population

The trial was carried out in 67 general practices across the Alsace region, all members of the General Medicine Department practice-based research network.

Patients included were aged 60 years or older, autonomous in their daily life, and had consulted their general practitioner for any reason. The minimum age limit was set at 60 because younger patients are less likely to suffer from cramps.[3,4]

The pools of cases and controls were generated during the consultation time. General practitioners recruited patients prospectively using a systematic step of 1 in 4 attending patients aged 60 years or older. Anonymized clinical data was collected with a screening questionnaire and entered into an electronic database for future contact. The existence of leg cramps was determined at the time of the consultation.

Case Control Matching

Cases were defined as patients aged 60 years and older currently having NLC. Controls were defined as patients free from any kind of rest cramps. Each case was matched with 1 control. Matching criteria were: same sex, same age group (age difference less than 5 years), with at least 1 of the following elements in common: 1 medication (Supplemental Appendix 1, available at http://www.annfammed.org/content/16/4/296/suppl/DC1/) or 1 medical condition (Supplemental Appendix 2, available at http://www.annfammed.org/content/16/4/296/suppl/DC1/) suspected of triggering cramps.[5,6,14,18]

Data Collection

We collected data at 2 different times. Initially, during the consultation time, clinical data from all eligible patients were recorded in a database under encoded numbers. Data included sex, age, medical history, medications, and characteristics of muscular cramps. Later, after case/control matching, investigators phoned the patients to schedule an interview to explain and administer the food frequency questionnaire. When patients were registered as lost to follow-up, a new matching was done when possible.

Measuring Instruments/Outcome Measures

The screening questionnaire was based on a literature review[4,5,7,8,22-24] and focused on demographics, cramp presence and main features, medical history, and treatments. The questionnaire was then evaluated by 8 general practitioners and amended. The final questionnaire was explicit in defining cramps as a painful involuntary muscle contraction when resting, lasting from a few seconds to a few minutes.[1-5,7,8,14,22]

The food frequency questionnaire appears to be the best method to evaluate individual dietary intake among general practice patients.[25] In this study, we used the food frequency questionnaire from the French Cohort Study (E3N) of the European Prospective Investigation into Diet and Cancer (EPIC) Study. The E3N food frequency questionnaire was validated to classify study subjects according to their food or nutrient intake over a 1-year period.[26,27]

The beverages explored by E3N food frequency questionnaire are presented in Supplemental Appendix 3, available at http://www.annfammed.org/content/16/4/296/suppl/DC1/. For each participant, we computed the total 1-week volume of alcoholic beverage from the 1-week consumption of each alcoholic beverage presented in Supplemental Appendix 3. Using a food and drink composition table, we converted the volumes to a 1-week mass of alcohol consumed.[28]

Patients were distributed into groups of consumers and nonconsumers of alcoholic beverage. When patients used an alcoholic beverage less than once a week, they were distributed in the nonconsumers group.

Statistical Analysis

We assumed that 67% of the controls were consuming alcohol once a week.[29] Therefore we calculated the sample size based on an assumed odds ratio of 3, with 80% power at a 5% level of significance. Given the fact that we carried out a case-control study with 1 case for each control, ignoring the clustering effect, we estimated that 76 subjects would be required in each group.

We compared consumers and nonconsumers of alcoholic beverages with Bayesian conditional logis-

tic and hierarchical linear regressions to take into account the matching. In the absence of an informative prior distribution based on the clinic, we used a normal distribution of the odds ratios of the association between the consumption of alcohol and the presence of cramps. We used a mean equal to 0 and a variance equal to 10 for conditional logistic regression and equal to 100 for linear regression. In order to confirm the robustness of the models, we performed sensibility analyses with all the data, by modifying the prior means and prior odds ratios and by creating hierarchical logistic models. For each model, 100,000 iterations were used after a burning of 10,000 iterations. The thinning used was 1. Convergence and auto-correlation were checked after each model.

Then, we explored the linear relationship between mass of alcohol consumption and odds of cramps with a Bayesian univariate and multivariate conditional logistic regression. We also computed credibility intervals and posterior probabilities. In a Bayesian approach a posterior probability (PP) below 95% means that no difference has been identified with sufficient probability.

Bayesian inference was chosen because this statistical method enables the inclusion of prior information. The parameter estimates are issued with credibility intervals, providing a more intuitive interpretation than the one that is almost always wrongly given when the (frequentist) confidence interval is used. The Bayesian approach is better adapted to studies where the amount of data are limited. The conclusions are formulated in terms of probability, taking into account the given data.[30-33]

All the analyses were performed with R 3.3.3 and WinBUGS software, version 1.4.3 (The BUGS Project, MRC Biostatistics Unit, University of Cambridge).[34]

RESULTS

Study Population Characteristics

Between January and June 2013, 849 patients were approached. From that group, 492 voluntary patients were listed in the database for further contact and of those, 222 subjects agreed to meet. From the collected questionnaires, we matched 70 pairs (Figure 1). Of the 70 pairs, 40 were men (57%). Patients were aged 60 to 86 years. The mean age (SD) was 67.8 (6.3) for cases and 67.9 (6.3) for controls. Cases and controls were similar according to age group, medications, and medical conditions (Table 1).

Consumption and Cramps

Among the 140 participants: 24 never consumed alcoholic beverages and 116 consumed alcoholic beverage on a regular basis. Weekly, cases consumed a median of 94 g of alcohol (interquartile range 211), while controls consumed 66 g (interquartile range 198) (Figure 2). The concordance or discordance between cases and controls for the consumption of alcohol is shown in Supplemental Table 1, http://www.annfammed.org/content/16/4/296/suppl/DC1/). Among the 70 pairs, 14 differed according to the consumption of alcoholic beverages.

We found an association between the global consumption of alcoholic beverages and NLC. Patients drinking alcohol at least once a week had an odds ratio of 6.5 of having cramps (95% credibility interval, 1.68-38.05; posterior probability 99.82%). There was no linear relationship between amount of alcohol used and odds of cramps. The odds ratios for an additional intake of 1 gram of alcohol were 1.001 for the univariate model and 1.000 for the multivariate model. Both had 95% creditability intervals of 0.98-1.01. The posterior probabilities were nonsignificant (under 95%).

DISCUSSION

Main Results

We found a strong association between the global consumption of alcoholic beverages and NLC. To the best of our knowledge, this is the first study to measure such a link.

Possible Explanations for the Association Between Alcohol Use and NLC

Alcohol consumption is responsible for many medical conditions, from gout[35,36] to heart attacks,[37] neuropathy, and myopathy.[38-40] We found only 2 reported cases of cramps, without any signs of myopathy, that were presumably due to the consumption of alcoholic

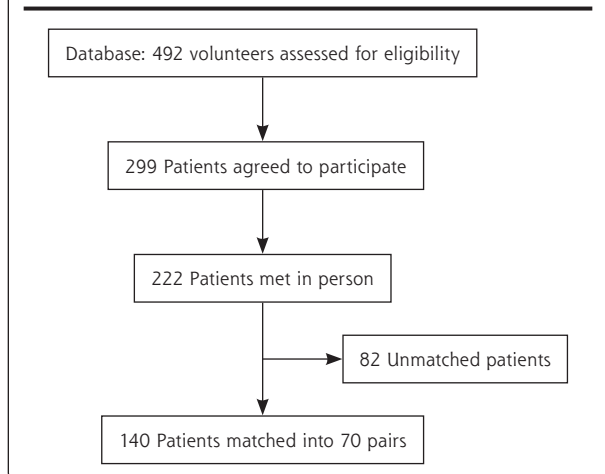**Figure 1. Study population screening, selection, and matching.**

Database: 492 volunteers assessed for eligibility

299 Patients agreed to participate

222 Patients met in person

82 Unmatched patients

140 Patients matched into 70 pairs

Table 1. Comparison of Age Groups, Medications, and Medical Conditions of Cases and Controls

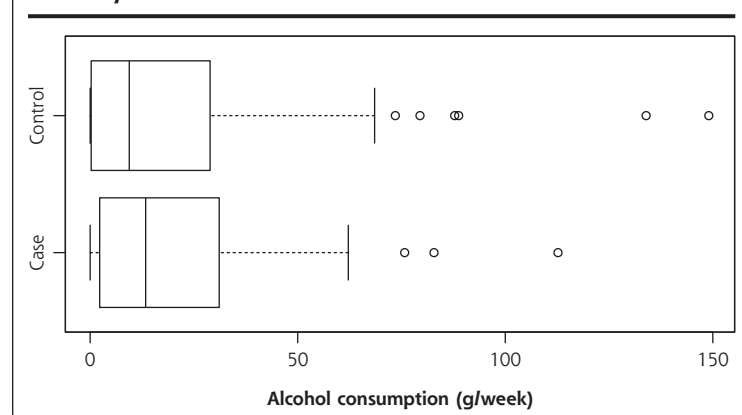|	Case	Control	P value[a]		Case	Control	P value[a]
Age Group							
60-64	26	27	.86	**Medication (continued)**			
65-69	20	18	.70	Others			
70-74	9	13	.35	Bisphosphonates	0	1	1
75-79	13	9	.35	Anti-epileptic drug	0	1	1
≥80	2	3	.65	NSAIDs	1	0	1
Medication				Proton pump inhibitor	11	11	1
No medication	15	13	.70	Alpha-blocker	3	0	.25
Anti hypertensive drugs				Melatonin	0	0	
Thiazides	2	4	.69	Progestogen	1	0	1
Calcium channel blockers	10	8	.63	Selective estrogen receptor modulator	0	0	
Beta-blockers	20	13	.21	GnRH analogue	0	0	
Loop diuretics	2	3	1	Others	88	92	.75
ACE/ARBs	18	11	.19	**Medical Conditions**			
Potassium-sparing diuretics	2	4	.69	Hypertension	51	49	.71
Centrally-acting agents	3	2	1	Severe arteriopathy	2	1	1
Association ACE/ARBs + thiazides	11	12	.82	Severe venous insufficiency	4	2	.68
Association ACE/ARBs + CCBs	5	2	.45	Diabetes	14	12	.66
Association beta-blockers + thiazides	0	3	.25	Hypothyroidy	9	7	.60
Lipid lowering drugs				Hypoparathyroidy	0	1	1
Statin	22	23	88	Severe renal insufficiency	6	1	.11
Ezetrol	0	0		Peripheral neuropathy	3	0	.24
Inhalated medication				Restless leg syndrome	1	0	1
Beta-mimetics	3	4	1	Alcohol addiction	0	2	.50
Anti-leukotriene	1	1	1	Cancer (not in remission)	2	2	1
				Others	55	59	.38

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; CCB = calcium channel blocker; GnRH = gonadatrophin-releasing hormone; NSAID = nonsteroidal anti-inflammatory drug.

[a] P value were calculated using a χ^2 test.

beverages.[20,41] Cramps are one of the symptoms of alcoholic myopathy and is characterized histologically by selective atrophy of type II fibers.[40,42] We hypothesize that, since the same defect is observed in aging individuals and in people with sedentary lifestyles,[43,44] chronic alcohol intake may increase the destruction of type II fibers in the elderly and make them more vulnerable to NLC.[40] This remains to be confirmed. To our knowledge, the literature does not provide any evidence linking alcoholic neuropathy and cramps. Binge drinkers seem to be more at risk for complications such as heart attacks than people who chronically consume alcohol.[37] Our study did not specifically explore the modality of alcohol intake, but binge drinking is rare among the elderly French population. An international multicenter cohort study would be necessary to confirm a causal link between alcohol consumption and NLC, and to determine a threshold for acute and chronic consumption.

Future Research and Implications for Practice

Further research should be undertaken to investigate the existence of an alcohol dose-related effect. Our study offers practitioners 2 major new elements for their daily practice. Advising patients about

Figure 2. Comparison of the mass of alcohol consumed per week by cases and controls.

the impact of alcohol consumption on NLC may be an effective way to prevent these painful episodes. Alternatively, discussing NLC may be another icebreaker for general practitioners to approach alcohol misuse.

Strengths and Limitations

Visual impairment, as well as the time needed to complete the questionnaire may have discouraged some participants, although the use of this auto-questionnaire had previously been validated.[27,45] The E3N food frequency questionnaire is a recall questionnaire administered at 1 time point, but its accuracy, the period of 1 month allocated to complete the questionnaire, and the aid of a research assistant before and after the data collection limit memory and lack of precision bias. Nevertheless, all the information remains declarative.

Our population includes a greater proportion of men than a standardized French population (Supplemental Table 2, http://www.annfammed.org/content/16/4/296/suppl/DC1). According to the literature, 79% of French men consume alcohol weekly while only 47% of women do the same.[29,46] The impact of the difference in gender remains unknown, but the matching based on gender aimed to minimize it.

In summary, to our knowledge, this study is the first to focus on the association between the global consumption of alcoholic beverages and NLC in a primary care environment. We found a strong association between the consumption of alcoholic beverages and NLC. More studies are needed to evaluate the existence of a causal link and to determine the pathophysiology of cramps and the impact of alcohol on it.

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