Available online at www.sciencedirect.com

ScienceDirect

Neuromuscular Disorders 24 (2014) 671–676

www.elsevier.com/locate/nmd

Characteristics of muscle cramps in patients with polyneuropathy

Sarah K. Maxwell [a], Seint Kokokyi [b], Ari Breiner [b,c], Hamid Ebadi [b,c], Vera Bril [b,c], Hans D. Katzberg [b,c,*]

[a] Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
[b] Division of Neurology, University Health Network, Toronto, Ontario, Canada
[c] Division of Neurology, University of Toronto, Toronto, Ontario, Canada

Received 3 March 2014; received in revised form 4 April 2014; accepted 24 April 2014

Abstract

Muscle cramps are common in the general population and can be disabling for patients, but there is little evidence comprehensively evaluating cramp characteristics in patients with polyneuropathy. This study describes the prevalence and characteristics of muscle cramps in this patient group. Patients over 18 diagnosed with polyneuropathy were invited to join the study. Patients completed nerve conduction studies, the Toronto Clinical Neuropathy score, neuropathy-specific Vickrey's Quality of Life Assessment and a self-administered questionnaire examining demographics, neuropathy symptoms and cramp characteristics. Two hundred and twenty-five participants were enrolled (28.0% female). Sixty-three percent of patients experienced cramps, occurring on average 6 times per week, lasting 10.5 min and scoring 6 out of 10 on a pain scale and described as disabling by 43.6% of patients. No significant difference was found in cramp prevalence according to underlying pathophysiology ($p = 0.52$) or fiber type ($p = 0.41$). Patients with disabling cramps rated their physical ($p < 0.0001$) and mental ($p = 0.04$) quality of life lower than patients without disabling cramps. This study confirms that muscle cramps are common, disabling and associated with reduced quality of life in patients with polyneuropathy. Similar prevalence of cramps across predominant nerve fiber type suggests a role of sensory afferents in cramp generation, although this needs to be confirmed in larger cohorts.

Keywords: Neuropathy; Muscle cramp; Nerve; Hyperexcitable; Motor

1. Introduction

Muscle cramps are sudden, involuntary, usually painful contractions of a muscle or muscle group. Cramps occur frequently in the general adult population [1,2] ranging from mild and infrequent to severe. In some patients, quality of life is reduced by interfering with sleep [3] as well as causing acute pain and soreness lasting days [4]. Although the mechanisms underlying development of muscle cramps are poorly understood, they are thought to be due to either to motor nerve hyper-excitability generated centrally at the spinal level or from aberrantly firing axons in the periphery [5]. Although motor axons are thought to be prominently involved in the generation of cramps, thinly or unmyelinated (A-delta and C) fibers are also present in muscle as afferents and may be involved in the pathogenesis of muscle cramps [6].

Muscle cramps may be idiopathic, usually in the form of nocturnal calf cramps in the elderly [2,7]. Cramps have also been reported in the presence of disease states such as nephropathy, cirrhosis, and particularly conditions affecting the peripheral nervous system such as polyneuropathy. For example, muscle cramps are

* Corresponding author at: Toronto General Hospital/UHN, 200 Elizabeth Street, 5ES-306, Toronto, Ontario M5G 2C4, Canada. Tel.: +1 (416) 340 3662; fax: +1 (416) 340 4081.
E-mail address: hans.katzberg@utoronto.ca (H.D. Katzberg).

http://dx.doi.org/10.1016/j.nmd.2014.04.008
0960-8966/

frequent in acquired neuropathy such as toxic neuropathy [8] and Guillian–Barré syndrome [9]. According to two studies [10,11], the presence and severity of cramps in patients with hereditary sensory and motor neuropathy (Charcot–Marie–Tooth disease) has been shown to be a strong independent predictor of reduced quality of life among other severe symptoms including weakness resulting in difficulty ambulating. Literature comprehensively evaluating prevalence and cramp characteristics in patients with polyneuropathy is limited [1,12]. The aim of our study is to determine the prevalence and characteristics of muscle cramps in this patient population. Treating muscle cramps are frequently challenging for both practitioners and patients. This information will help guide adequate and timely treatment of this under-recognized symptom using available evidence based [13] and patient-centered [14] approaches to treatment.

2. Materials and methods

2.1. Subjects

The study was approved by the research ethics board of the University Health Network (Toronto, Ontario, Canada). Patients with a diagnosis of polyneuropathy were recruited from the Prosserman Family Neuromuscular Clinic at the University Health Network from January 2011 to September 2013 using a convenience, consecutive sampling method. This clinic is a tertiary referral center for the diagnosis and treatment of neuromuscular disorders, including polyneuropathy. Polyneuropathy was diagnosed on clinical grounds based on symptoms and clinical examination findings. Symptoms may include neuropathic pain, sensory disturbances, muscle cramps and weakness; physical examination findings may include sensory disturbances, weakness, and hyporeflexia, as determined by a neuromuscular specialist. Ancillary tests included nerve conduction studies [15] and electromyography, and laboratory, or genetic tests. Abnormal sural nerve biopsy was also accepted to confirm the presence of polyneuropathy but not required. Patients were classified according to etiology for example: diabetes, chronic inflammatory demyelinating polyradiculopathy (CIDP), multifocal motor neuropathy (MMN), idiopathic, paraprotein, hereditary, toxic, nutritional, Guillian–Barré syndrome (GBS), and human immunodeficiency virus (HIV). After providing informed consent, patients completed a symptom questionnaire related to muscle cramps and other symptoms of polyneuropathy. Patient charts and study surveys were accessed by a research assistant and data entered into a secure database.

2.2. Measurements

2.2.1. Cramp and symptom survey

Cramps were defined as involuntary, painful muscle contractions. Patients were asked to rate the frequency of cramps (number of times per week), severity of pain associated with cramps at the time of the event (not severe = 0 to very severe = 10) on an 11-point Likert scale, duration of cramps (minutes) and whether they considered their cramps disabling (yes or no). Patients were asked to rate their neuropathic pain associated with muscle cramps separately from 0 to 10 (no pain = 0, severe pain = 10) on an 11-point Likert scale. Lastly, each patient completed the Vickrey Peripheral Neuropathy Quality of Life Instrument-97 [13] which assesses health related quality of life specific to polyneuropathy along physical and mental health domains.

2.2.2. Toronto Clinical Neuropathy Score

The Toronto Clinical Neuropathy Score (TCNS) is a valid and reliable tool to assess the presence and severity polyneuropathy and was used to grade the severity of polyneuropathy in our cohort [16,17]. The TCNS total is a continuous score that ranges from 0 (no symptoms or signs of neuropathy) to a maximum of 19 [17] and can further be defined as: no neuropathy (0–5), mild (6–8), moderate (9–11) or severe neuropathy ($\geqslant$12) [18,19].

2.2.3. Nerve conduction studies

Nerve conduction studies were obtained from patient medical records. The NCS were performed using surface stimulating and recording techniques, according to specifications of the American Association of Electrodiagnostic Medicine [13] and the Canadian Society of Clinical Neurophysiology [20]. All studies were conducted by either a trained technician or a neurologist specialized in electrodiagnostic medicine. Sural sensory, peroneal and tibial motor nerve latencies, amplitudes and conduction velocities were measured. Upper extremity median and ulnar motor and sensory nerve conduction studies were performed. Demyelinating neuropathy was defined according to the Koski electrophysiologic criteria [21].

2.2.4. Classification of polyneuropathy

Polyneuropathy was further classified clinically based on the predominant nerve fiber type involved as either (1) sensorimotor, (2) ganglionopathy, (3) pure motor or (4) small fiber [22]. Patients were classified as having small fiber polyneuropathy when they presented with abnormal sensory symptoms (burning or lancinating pain and dysthesias), at least one abnormal paraclinical tests such as sympathetic skin response, R–R interval testing, quantitative sensory testing of cold and heat detection, cutaneous axon-mediated laser Doppler flare imaging, corneal confocal microscopy or reduced intraepidermal nerve fiber density on skin punch biopsy in the presence of normal nerve conduction studies [23]. Sensory ganglionopathy was diagnosed in those patients having prominent sensory disturbances including the presence of sensory ataxia in addition to: (1) abnormal sensory responses on nerve conduction studies (2) no weakness, atrophy or deformity on examination (3) normal motor responses on NCS and EMG. Patients with pure