ORIGINAL ARTICLE

Chronic Pain in Persons With Myotonic Dystrophy and Facioscapulohumeral Dystrophy

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ABSTRACT. Jensen MP, Hoffman AJ, Stoelb BL, Abresch RT, Carter GT, McDonald CM. Chronic pain in persons with myotonic dystrophy and facioscapulohumeral dystrophy. Arch Phys Med Rehabil 2008;89:320-8.

Objective: To determine the nature and scope of pain in working-aged adults with myotonic muscular dystrophy (MMD) and facioscapulohumeral muscular dystrophy (FSHD).

Design: Retrospective, cross-sectional survey.

Setting: Community-based survey.

Participants: Convenience sample of subjects with MMD and FSHD.

Interventions: Not applicable.

Main Outcome Measures: Overall intensity and duration of pain, pain inference, pain sites, pain treatments, and relief provided by pain treatments.

Results: More subjects with FSHD (82%) than with MMD (64%) reported pain. The most frequently reported pain sites for both diagnostic groups were lower back (66% MMD, 74% FSHD) and legs (60% MMD, 72% FSHD). Significant differences in pain intensity were found between the diagnostic groups in the hands, legs, knees, ankles, and feet, with patients with MMD reporting greater pain intensity at these sites than patients with FSHD. Age was related to the onset of pain (participants reporting pain were younger than those not reporting pain in the FSHD sample), but pain severity was not significantly associated with age in those reporting pain. Respondents with both diagnoses that reported mobility limitations and used assistive devices (eg, wheelchair, cane) reported more pain severity than those with mobility limitations who did not use assistive devices, who, in turn, reported more pain severity than respondents who reported no mobility limitations at all. The treatments that were reported to provide the greatest pain relief were not necessarily those that were the most frequently tried or still used.

Conclusions: The findings indicate that pain is a more common problem in persons with FSHD than in persons with MMD, although it is common in both populations. In addition, these pain problems are chronic, underscoring the need to identify and provide effective pain treatments for patients with these neuromuscular diseases.

Key Words: Facioscapulohumeral muscular dystrophy; Myotonic dystrophy; Pain; Rehabilitation.

RECENT RESEARCH SUGGESTS that chronic pain may be a significant problem in many persons with chronic neuromuscular disease (NMD), including all forms of muscular dystrophy. Muscular dystrophy (MD) is a group of genetically distinct disorders characterized by progressive weakness and dystrophic changes in muscle with loss of normal muscle fibers and replacement with fat and connective tissue. Two of the most common forms of MD seen in adults are myotonic muscular dystrophy (MMD) and facioscapulohumeral muscular dystrophy (FSHD); they are the focus of this study.

There are 2 known forms of adult MMD. Type 2 MMD (MMD2 or DM2) is much less common than type 1 MMD and is also referred to as proximal myotonic myopathy. DM2 is caused by a mutation on chromosome 3 and is clinically less severe than either typical MMD (DM1) or congenital MMD, which is the childhood form of this disease.[1] DM1, referred to as MMD hereafter, is an autosomal dominant, multisystem muscular dystrophy with an incidence of 1 per 8000.[2,3] All of the MMD participants in this study have DM1, which is a multisystem disorder affecting skeletal muscle, smooth muscle, myocardium, brain, and ocular structures. Associated findings include frontal pattern baldness and gonadal atrophy (in males), cataracts, and cardiac dysrhythmias. Because of insulin insensitivity, MMD patients have a high risk for developing type 2 diabetes mellitus. The gene has been localized to an unstable CTG trinucleotide repeat within the region of the DM protein kinase locus at 19q13.3.[4,5] MMD patients may have 50 to several thousand CTG repeats, with a tendency toward increased repeats with successive generations. The age of onset is inversely correlated by the size of the CTG repeats.[4] Classic, young adult-onset MMD shows 100 to 1000 repeats. Several characteristic facial features of MMD may be seen, including frontal balding and temporal wasting. MMD is one of the few dystrophic myopathies with greater distal weakness than proximal weakness.[6] Although neck flexors, shoulder girdle musculature, and pelvic girdle musculature can become significantly involved over decades, the weakness is initially most predominant in the ankle dorsiflexors, ankle everters and inverters, and hand muscles.[3] Significant muscle wasting can occur over time. MMD patients may experience painful muscle cramping because of myotonia, which is delayed relaxation or sustained contraction of the muscle fibers. Grip myotonia can be shown by delayed opening of the hand with difficulty extending the fingers after tight grip. Percussion myotonia can be elicited by striking the thenar eminence with a reflex hammer, producing adduction and flexion of the thumb with slow return. Needle electromyography shows myotonic discharges,

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which are spontaneous waxing and waning spikes that produce a characteristic "dive bomber" sound.[7] Cardiac abnormalities are present in 70% to 75% of patients with MMD.[3,8,9] Weakness in the respiratory muscles is a major cause of morbidity. Also, constipation is fairly common because of smooth muscle involvement. Adult-onset MMD patients frequently have a generally lower intelligence than normal, with full-scale intelligence quotient reported to be in the 86 to 92 range.[3] Cognitive functioning also appears to be directly related to the size of the CTG expansion at the MMD gene locus.

FSHD, also referred to as Landouzy-Déjérine disease, is a slowly progressive dystrophic myopathy with predominant involvement of facial and shoulder girdle musculature. FSHD has a worldwide prevalence estimated at 10 to 20 per million.[2,10] FSHD is caused by a deletion on the chromosome 4q35 locus and is transmitted in an autosomal dominant fashion.[1,11-13] Prominent facial weakness is the hallmark of FSHD. These patients often have difficulty with eye closure and may appear expressionless. They have difficulty whistling, pursing the lips, drinking through a straw, or smiling. Oddly, masseter, temporalis, extraocular, and pharyngeal muscles characteristically are spared in FSHD. Weakness in the trapezius, rhomboids, latissimus dorsi, and serratus anterior muscles result in the scapula being positioned laterally and superiorly, with the shoulders forward sloped. This may produce posterior and lateral scapular winging. Unlike other dystrophies, the musculature involvement in FSHD may be quite asymmetric. Other comorbid problems seen in FSHD include a sensory neural hearing deficit and telangiectasia of the retina. Although limb-joint contractures are uncommon in FSHD, spinal deformity is common, usually hyperlordosis, alone or in combination with scoliosis. Cardiac and respiratory problems are rare in FSHD.

Recent preliminary research suggests that pain may be a significant problem for many persons with MMD and FSHD. For example, Bushby et al[14] recently reported on 4 subjects with FSHD who identified pain as their most disabling symptom and complained of between 3 to 7 separate pain complaints. In addition, Abresch et al[15] found that 83% of a sample of 811 subjects with various NMDs, including 64 persons with FSHD and 33 with MMD, reported at least some ongoing pain problems. Moreover, the frequency and severity of pain in their combined sample of patients with FSHD, MMD, and a sample of patients with limb-girdle syndrome was significantly greater than levels of pain reported by the general U.S. population. Finally, our group recently surveyed 193 subjects with a variety of NMDs, including 18 patients with FSHD and 26 patients with MMD, and found that 73% of the sample as a whole (89% of patients with FSHD, 69% of those with MMD) reported pain problems, with 27% of the overall sample reporting severe pain (19% of patients with FSHD, 50% of patients with MMD).[16] We found that pain was reported to interfere moderately with a number of activities of daily living across all of the NMD diagnostic groups (range of interference ratings, 2.6–4.63 on 0–10 interference ratings scales) and to occur all over the body (least common, abdomen, and/or pelvis at 16%; most common, back at 49%). Medications were the most common pain treatment used by these patients, with ibuprofen, aspirin, acetaminophen, opioids, gabapentin (Neurontin), and muscle relaxants the most common, and all used by 50% or more of the patients with pain. However, we were unable to examine pain interference, pain sites, and pain treatments as a function of diagnostic group because of the low sample sizes of the individual NMD diagnostic groups in our previous study.[16]

Although the preliminary findings from our group and others indicate that chronic pain can be a serious problem for many persons with FSHD and MMD, much remains unknown about the nature and scope of pain in these patient populations. Importantly, most of the research on pain that has been performed with patients with FSHD and MMD has reported findings from a mixed population of patients with limited sample sizes for particular diagnoses. This limits both the reliability and generalizability of the available findings. Descriptive analyses regarding pain with larger samples of patients with specific diagnoses would provide for greater reliability of the findings and would allow us to confirm (or question) previously published data concerning pain in patients with these conditions. Moreover, because both FSHD and MMD are progressive diseases, it is possible that the onset of pain and the severity of pain once it develops may be related to a patient's age or degree of mobility impairment. This study sought to address the need for more information about the nature and scope of pain in persons with FSHD and MMD.

METHODS

Participants

The research methodology and all the study protocols were approved by the University of Washington Human Subjects Committee. Participants were recruited from the following sources: the National Registry of Myotonic Dystrophy and Facioscapulohumeral Muscular Dystrophy Patients and Family Members (*http://www.urmc.rochester.edu/nihregistry/*) (n=296) funded by the National Institutes of Health, the University of Washington NMD Clinic list (n=87), the Quality of Life Pediatric Survey Study (n=8), and 4 participants who independently contacted study personnel. In total, 395 surveys were mailed out to persons living with NMD. Of those 395 surveys sent, 2 were returned because the participant no longer lived at the address on record, 6 were deceased, and 5 were returned as ineligible (no NMD diagnosis or <18 years of age). Of the remaining 382 surveys, 298 were returned, yielding a survey return rate of 78%. Data from 5 of these surveys could not be analyzed (because of insufficient data or ineligibility) and were consequently excluded from further analysis. The current sample includes only participants with MMD and FSHD (n=257). Because the majority of these participants were recruited through the National Registry, that protocol is as follows: individuals who have been diagnosed with FSHD or MMD by a neuromuscular specialist contact the Registry and provide the Registry with demographic information and permission to access their medical records. The Registry then abstracts and deidentifies the information in the medical records and assists with subject recruitment. Inclusion criteria for this study included the following: (1) primary diagnosis of MMD or FSHD, (2) chronologic age of 18 or older (ie, working-aged adults), and (3) ability to read and write English. On approval of the proposed study by the Scientific Advisory Committee of the Registry, the data manager extracted potentially eligible members from the database and wrote them a letter informing the prospective subjects about the study. Members of the Registry were instructed to call or e-mail research personnel if they were interested in participating. A total of 296 potential subjects with MMD or FSHD contacted us. Of these, 235 (93%) completed and returned a mail survey questionnaire on the nature and scope of their pain.

Approximately half (50.6%) of the sample was diagnosed with MMD and half (49.4%) with FSHD. Fifty-one percent of the sample reported having received a deoxyribonucleic acid (DNA) confirmation of NMD diagnosis.

Measures

The survey included questions asking about demographic information, NMD-related information, pain intensity, pain interference, pain location, and pain treatments.