Non-dystrophic myotonic disorders: Patients' Insights on Treatment Access

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Background

Non-dystrophic myotonic disorders (NDM) are rare, genetic diseases that arise from mutations in skeletal muscle chloride and sodium ion channels resulting in disabling altered membrane excitability causing prolonged muscle contraction and delayed relaxation [1,2]. The myotonia can be dramatic and disabling. Triggers for myotonia include [3,4] :

- Emotional surprises
- Cold
- Exercise, and rest after exercise
- Stress
- Potassium (potassium-rich foods)
- Alcohol

The onset of symptoms is unpredictable [2,6]. The major clinical manifestation of myotonia is muscle stiffness. Patients also experience pain, weakness, impaired mobility, affected speech and may have a higher risk of falling [5, 7]. Myotonia can also affect muscles of mastication and swallowing [2,8].

The NDM disorders are each genetically different, have distinctive clinical findings and include [9]:

- Sodium channelopathies:
  - Paramyotonia congenita
  - Hyperkalaemic periodic paralysis with myotonia
  - Potassium-aggravated myotonia (myotonia permanens, myotonia fluctuans, acetazolamide-responsive myotonia)
- Chloride channelopathies (myotonia congenita (MC)):
  - Thomsen myotonia
  - Becker myotonia.

Quality of life (QoL) is compromised by the unpredictable frequency and severity of myotonic episodes associated with life-long symptoms and negative impact on physical functioning. Treatment options are limited, and have included unlicensed products such as mexiletine. However, Namuscla® (mexiletine 167mg) obtained marketing authorisation by the European Medicines Agency in December 2018 [9].

Aims

This survey, conducted between January and March 2018 in 13 European countries, sought to evaluate the awareness and access to mexiletine and subsequent harm caused by limited treatment access.

Methods

The Myotonia Observation Survey of Patient Access to Therapy avoiding Harm (MyoPath) survey was conducted as a mixed-methods survey consisting of:

- Qualitative semi-structured interviews with patient organisations or independent patient representatives and myotonia specialists. The interviews, using a bespoke questionnaire [10], were focused on obtaining data on the overall treatment of NDM, and the outcomes for patients not having access to treatment.
- Quantitative online-survey [11] that was aimed at verifying the data collected in the interviews and further establishing the diagnosis, symptoms, treatments and access to treatments for patients with NDM.

Results

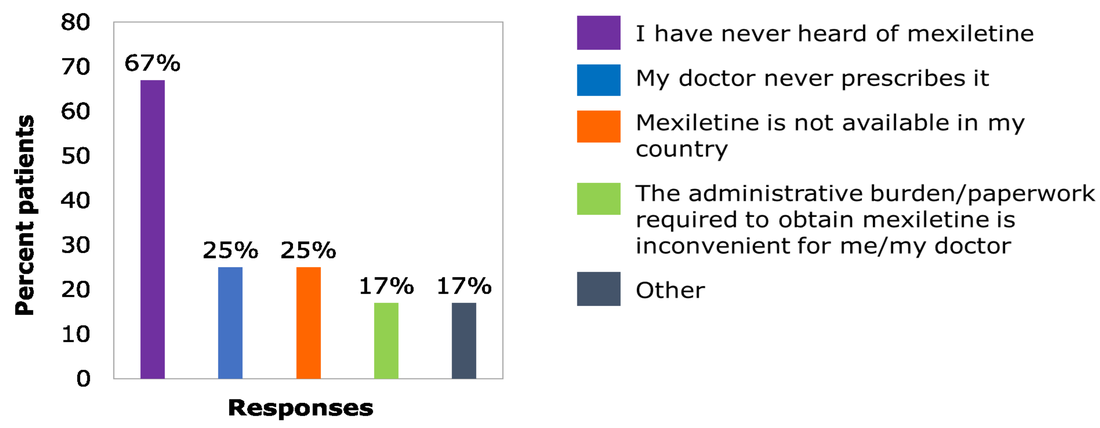
The online patient survey included 37 participants with confirmed MC in 6 European countries. Of the patients taking mexiletine, 84% had been prescribed mexiletine by a neurologist. Other patients were prescribed mexiletine by cardiologists, general practitioners, ophthalmologists, pneumologist and rheumatologists. Difficulty in obtaining mexiletine was experienced (multiple answers applied to some patients) as :

Mexiletine is not available at a local pharmacy	80%
I have to visit my doctor/ centre of expertise/hospital frequently to get a prescription/refill of mexiletine	53%
I have to travel a long distance to visit my doctor/ centre of expertise/ hospital to get a prescription for mexiletine/refill	60%
The administrative burden/paperwork required to get mexiletine is inconvenient for me and/or my doctor	53%
The packaging and prescription information for mexiletine are not in my native language	73%
I have to wait a long time to receive mexiletine	60%
My doctor could not prescribe mexiletine (either because it's not available in my country/other reason)	40%
My health insurance does not reimburse me for the cost of mexiletine (or only to a limited extent)	7%
The product is inconsistent or confusing (not always from the same manufacturer or different dosing strengths. E.g 50mg vs. 200mg)	13%

Results

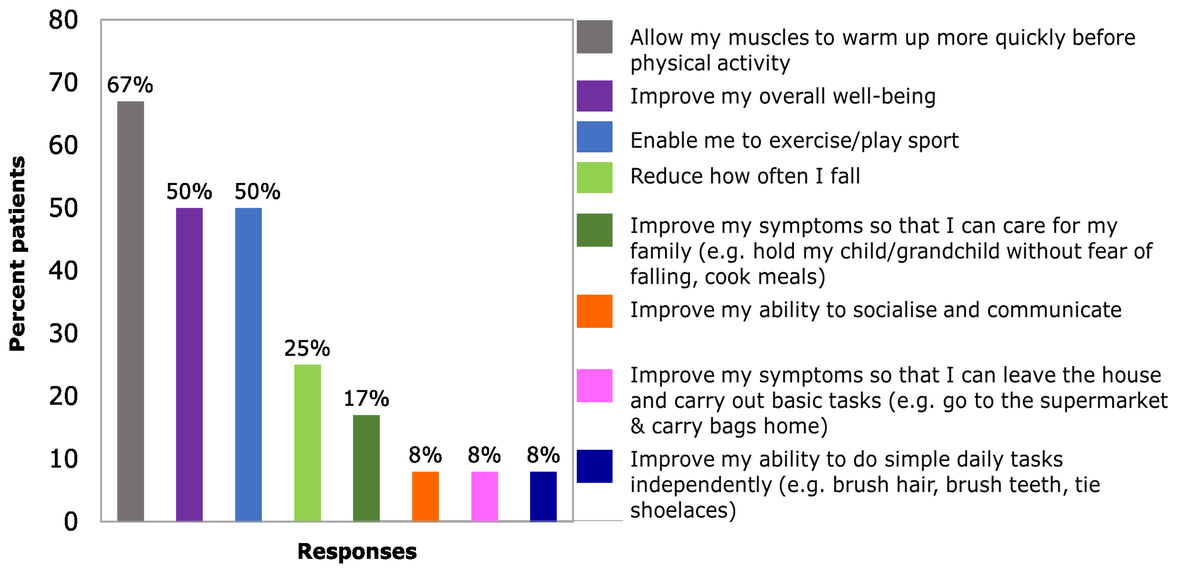
The qualitative findings identified that only 41% of patients with MC were receiving mexiletine at the time of the survey, while a further 27% were aware of mexiletine but were not being treated with it. An additional 27% of patients with MC did not take any medication to relieve the symptoms of myotonia. The reasons for patients not taking mexiletine are shown in Figure 1. Notably, 67% of the MC patients had not heard of mexiletine, and 25% of the patients explained that mexiletine is not available in their countries.

Figure 1. Reasons for not taking mexiletine (N = 12)



The quantitative outcomes are shown in Figure 2 that describes the important need for treatment so that patients with MC can perform daily functions and experience an improvement in overall well-being.

Figure 2. Reasons for treatment of myotonia (N =12)



A disruption in access to treatment caused harm in 85% of patients with MC resulting in 31% and 23% of patients experiencing "*drastic change*" and "*significant change*" in time needed for muscle warm-up, respectively. Lack of treatment with mexiletine resulted in similarly severe negative impact on other symptoms. Difficulty in obtaining mexiletine was experienced by 53% of the patients. Patients who had access to treatment with mexiletine expressed substantial benefits, with 36% and 55% of patients reporting a "drastic improvement" in the ability to work and in emotional well-being, respectively. Importantly, none of the patients felt that their symptoms were managed well with another therapy.

Patients (87%) expressed anxiety that mexiletine would not be available in the future, and 53% of the patients complained that they had to spend too much time obtaining mexiletine.

Discussion and Conclusion

The small number of patients is a limitation of this survey. However, as noted in the report by the Committee for Orphan Medicinal Products (COMP), based on the survey respondents who had experience with mexiletine, the impact of these patients' insights (gathered from the semi-structured interviews and online patient survey results) established the 'implied' harm to patients who did not have access to mexiletine [12] .A lack of awareness of mexiletine as a treatment option, a lack of access to treatment or treatment interruption which might be due to the absence of a licensed product in Europe have contributed to a negative impact on patients with NDM.

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