years. We hereby report the earliest "myopathy onset" ever described, enlarging the phenotypical spectrum of *CACNA1S*-related myopathies and suggest considering it even in young adult-onset myopathies, especially when granular vacuoles are present.

http://dx.doi.org/10.1016/j.nmd.2021.07.249

EP.226

Muscle fat fraction, cross-sectional area and contractility in patient with skeletal muscle sodium channel disorders

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We present a cross-sectional, observational study that investigates the presence of muscle degeneration in patients with skeletal muscle sodium channel disorders (*SCN4A* gene mutation). This includes paramyotonia congenita (PMC), hyperkalemic periodic paralysis (HyperPP) and potassium-aggravated myotonia (PAM). Little is known about quantitative fat infiltration and contractility of patients with these disorders. So far, we have studied 13 patients (30 planned), older than 18 years and diagnosed with *SCN4A* mutations using dynamometry testing and quantitative (Dixon) muscle MRI. Maximal isometric muscle strength (peak torque (PT) in Newton-meter (Nm)) of the lower limb knee and ankle flexors and extensors are measured using stationary dynamometry. Hand flexor strength of upper limb is measured using hand-held dynamometry. Dixon-MRI allows for quantitative calculation of fat fraction and cross-sectional area in respective muscles. Contractility is measured by comparing contractile cross-sectional area (CSSA) with peak torque. Preliminary results show irreversible fat replacement in patients: hand flexors 0/13, anterior group thigh 1/13, posterior group thigh 10/13, medial group thigh 4/13, gastrocnemius medialis 10/13, gastrocnemius lateralis 8/13, soleus 6/13, and anterior group calf 2/13. In patient with *SCN4A* mutations, our findings suggest irreversible fatty degeneration of muscles, particularly of the posterior group of the thigh and gastrocnemii muscles. The impact on muscle contractility and quantitative assessment of muscle fat fractions will be communicated at the meeting.

http://dx.doi.org/10.1016/j.nmd.2021.07.250

EP.227

Novel compound heterozygous mutations in *CLCN1* in a patient with myotonia congenita

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Myotonia congenita (MC) is a rare hereditary chloride channel neuromuscular disorder. It caused by *CLCN1* mutations which encodes chloride channel CLC1 for skeletal muscle. MC is characterized by transient muscle weakness, generalized muscle hypertrophy, non-progressive painless myotonia, and impaired muscle relaxation after contraction which resulting in muscle stiffness. We report a clinical case of an affected 14-year-old boy with athletic appearance due to generalized muscle hypertrophy, calf and brachial muscle stiffness, weakness especially in the legs, and normal deep tendon reflexes. He was born after uneventful pregnancy and delivery, with non-consanguineous marriage of his parents. There was no family history of neuromuscular disorders. He had numbness in the legs, getting tired quickly while walking, difficulties in starting voluntary activities such as walking and running. He had also delayed relaxation of hand grip after forceful holding. The neurological examination showed percussion-activated myotonia in the tongue, upper arms and legs. Plasma creatine kinase level was mildly elevated (200 UI/L, reference range: 0-190 UI/L), and transaminase levels were normal. We identified novel compound heterozygous mutations of *CLCN1* [c.1673C>T (p.Pro558Leu) in exon 15, paternal and c.1886T>C (p.Leu629Pro) in exon 16, maternal] with next generation sequencing. Molecular genetic analysis is an accurate option for diagnosing MC. The present case expands the genotypic spectrum of MC.

http://dx.doi.org/10.1016/j.nmd.2021.07.251

EP.228

Efficacy and safety of mexiletine in non-dystrophic myotonias: a randomized, double-blind, placebo-controlled, cross-over study

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Mexiletine – a non-selective voltage-gated sodium channel blocker – is one of the most effective treatments available for patients with non-dystrophic myotonias but has been prescribed off-label for more than 30 years. We investigated the efficacy and safety of MEXiletine in non-dystrophic MYOtonias in a randomized clinical trial (MYOMEX). The MYOMEX study was a multicenter, double-blind, placebo-controlled, cross over study aimed at patients with genetically defined myotonia congenita (MC) and paramyotonia congenita (PC). The primary endpoint was the self-reported score of stiffness severity on a 100-mm visual analogic scale (VAS). Mexiletine was started at 200 mg/day and titrated by increments of 200 mg every three days to reach a maximum dose of 600 mg/day in one week for a total treatment duration of 18 days for each cross-over period. The modified intent-to-treat population included 25 patients (13 with MC and 12 with PC; mean age, 43.0 years; male, 68.0%). The median stiffness VAS score for patients receiving mexiletine was 71.0 at baseline and decreased to 16.0 at the end of the treatment period while the score did not change for placebo (81.0 at baseline *vs*. 78.0 at end of treatment). A mixed effects linear model analysis on ranked absolute changes showed a significant effect of treatment ($p<0.001$). The overall quality of life score of the Individualized Neuromuscular Quality of Life questionnaire (INQoL) was significantly improved ($p<0.001$) and significant treatment effect was observed on all INQoL domains. No clinically significant adverse events or ECG conduction abnormalities were reported in this study. The MYOMEX study provides evidence that mexiletine significantly reduces myotonia in non-dystrophic myotonias independent of the type of channelopathy and is well tolerated.

http://dx.doi.org/10.1016/j.nmd.2021.07.252

MYOTONIC DYSTROPHY

EP.229

Characterising myotonic dystrophy (DM) and supporting national and international research projects: nine years of the UK DM patient registry

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