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Brief Communication

# Quality of life and excessive daytime sleepiness in children and adolescents with myotonic dystrophy type 1

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ABSTRACT

*Objectives:* Myotonic dystrophy type 1 (DM1) is an autosomal dominant neuromuscular disease with variable severity that affects all ages. Sleepiness is an important co-morbidity affecting a large proportion of paediatric DM1 patients. The current study examined the relationship between sleepiness and quality of life in a paediatric DM1 cohort.

*Methods:* A cross-sectional study was conducted in children and adolescents with DM1 attending a multi-disciplinary neuromuscular clinic in a tertiary paediatric centre. The modified Epworth sleepiness scale (ESS), the PedsQL™ quality of life (version 4.0) and neuromuscular modules (version 3.0) were used to measure sleepiness, generic quality of life and neuromuscular-specific quality of life, respectively.

*Results:* Seventeen current patients with DM1 completed all questionnaires and assessments. Of them, 35.5% had abnormal scores on the modified ESS, which is indicative of excessive daytime sleepiness (EDS). Higher ESS scores were highly significantly related to reduced quality of life in neuromuscular-specific ($r = 0.77$, $p < 0.001$) and generic measures ($r = 0.78$, $p < 0.001$). EDS was not significantly related to intellectual function or sleep disorders as detected on polysomnography.

*Conclusions:* EDS is common in children and adolescents with DM1. It is associated with reduced quality of life and should be routinely assessed. Further studies to develop treatments of EDS in this population are required and may improve overall outcomes.



## 1. Introduction

Myotonic dystrophy type 1 (DM1) is a multi-system disease with a broad spectrum of severity that arises from an autosomal dominant expansion of a CTG trinucleotide repeat in the non-coding region of the dystrophia myotonia gene (*DMPK*) [1]. DM1 is divided into pre-mutation, mild adult, classic, childhood and congenital forms depending on the age of onset. DM1 is the most common adult-onset muscular dystrophy, with a worldwide prevalence of approximately one in 8000 [2]. Clinical effects include progressive muscle weakness, myotonia, sleep problems and intellectual impairment.

Sleep problems, including excessive daytime sleepiness (EDS) and fatigue, are prominent non-muscular complaints in DM1 patients and present in approximately 80% of adults and 50% of children with DM1 [3,4]. EDS is characterised by persistent sleepiness, more likely during situations requiring less attention, and is not improved by naps [3]. The pathophysiology of sleep disorders in DM1 is complex and multi-factorial, including respiratory muscular weakness, central and obstructive sleep apnoea, restless leg syndrome/periodic limb movements and rapid eye movement (REM) sleep dysregulation [4–6]. Furthermore, DM1-associated EDS may be primarily caused by neurodegeneration within the brainstem reticular activating system, which leads to central dysfunction of sleep regulation [7].

*Abbreviations:* CDM1, Congenital Myotonic Dystrophy; DM1, Myotonic Dystrophy Type 1; DMPK, Dystrophia Myotonica protein kinase; ESS, Epworth Sleepiness Scale; EDS, Excessive Daytime Sleepiness; HRQOL, Health-related Quality of Life; JDM1, childhood/juvenile-onset Myotonic Dystrophy; MSLT, Multiple Sleep Latency Test; OSA, Obstructive Sleep Apnoea; PCR, Polymerase Chain Reaction; PSG, Polysomnography.

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There is a paucity of studies in the literature examining the relationship between sleepiness, quality of life, neuromuscular function and intellectual function in children with DM1. The present study describes the prevalence of EDS in a paediatric DM1 cohort and its association with quality of life.

## 2. Methods

This was a cross-sectional study of paediatric patients (aged 2–18 years) with DM1 who attended the Sydney Children's Hospital neuromuscular clinic for routine clinical care in 2015. All patients were eligible if they or their carers could communicate sufficient English language without the aid of an interpreter. The diagnosis was confirmed by triplet repeat primed PCR demonstrating an expanded CTG repeat in the DMPK gene on chromosome 19 and/or Southern blot for the quantitation of triplet repeats. The classification of DM1 was based on age of onset of clinical symptoms as follows: congenital myotonic dystrophy (CDM1) patients had clinical symptoms evident before the age of 12 months; childhood/juvenile-onset DM1 (JDM1) manifested symptoms after the first year of life.

Prospective cross-sectional assessments of sleepiness and generic and neuromuscular-specific quality of life were undertaken in the current DM1 patients. Polysomnography was conducted on the grounds of clinical suspicion of sleep-disordered breathing: habitual snoring, observed apnoea, recurrent respiratory tract infections, restless sleep or daytime sleepiness. Multiple sleep latency tests (MSLTs) were performed if needed to rule out narcolepsy. Individual daytime sleepiness was measured using the modified Epworth sleepiness scale (ESS), a questionnaire that asks the subject to score (from zero to three) their likelihood of falling asleep in eight routine life situations [8]. The modified version adopts scenarios that are more relevant to children. The average score among normal controls is 5.9 (SD 2.2), and in general, scores >8 indicate excessive sleepiness, with scores >10 generally accepted as indicating EDS [8]. The PedsQL™ quality of life (version 4.0) and neuromuscular modules (version 3.0) were used to measure the quality of life in generic and disease-specific approaches, respectively. These multi-dimensional scales assess the frequency of health problems within the past month. Children or parent proxies self-report a score of zero to four (never to almost always), and questionnaires are tailored to age groups of toddlers (ages two to four), young children (ages five to seven), children (ages 8–12) and teens (ages 13–18). The quality of life module consists of 23 questions that are further divided into physical, emotional, social and school functioning sub-sets. The 25-question PedsQL™ neuromuscular module was created as a more specific tool to measure health-related quality of life (HRQOL) for musculoskeletal diseases such as Duchenne's muscular dystrophy and spinal muscular atrophy [9,10]. It is sub-divided into symptom/function, communication and family resource dimensions. Greater scores indicate morbidity and illness burden than in healthy controls, the latter scoring no less than 80 in all scales [11]. Intellectual function was determined in our cohort by assessments including the Wechsler intelligence scale for children (WISC) [12] and the Griffiths mental development scales [13].

The South Eastern Sydney and Illawarra Area Health Service Human Research Ethics Committee approved this study.

## 3. Data analysis

Descriptive statistics were used to describe clinical features by sub-type and expressed as number (percentage) and mean ± standard deviation (SD). Cross-sectional data of the study was normally distributed and analysed using IBM SPSS version 22. To determine the relationship between sleepiness and HRQOL, simple linear regression was performed between the ESS and both the PedsQL™ quality of life and neuromuscular module.

**Table 1**
Clinical and sleep medicine assessment findings in 17 DM1 patients.

| Patient number | Age (years) | Current medications | Indication for sleep study | Sleep study results | Epworth sleep score | Subjective report of EDS | Cognitive function |
|---|---|---|---|---|---|---|---|
| 1 | 2 | | | | 2 | None | Normal |
| 2 | 3 | | | | 3 | None | Mild ID |
| 3 | 5 | Osmolax | | | 1 | None | Normal |
| 4 | 8 | | | | 0 | None | Severe ID |
| 5 | 8 | Osmolax, vitamin D | Snoring | Normal (AHI<1, no hypoventilation, no PLMs) | 16 | None | Mild ID |
| 6 | 9 | | | | 5 | None | Mild ID |
| 7 | 11 | Clonidine, carbamazepine, levetiracetam | Daytime somnolence, sleep fragmentation | Attempted but uncooperative | 17 | Moderate | Severe ID |
| 8 | 12 | Fluticasone | Daytime somnolence | Normal | 12 | Mild | Mild ID |
| 9 | 13 | | | | 3 | None | Mild ID |
| 10 | 14 | | Daytime somnolence | PLM index 19/hr | 6 | Moderate | Mild ID |
| 11 | 14 | | Titration study for nocturnal bi-level ventilation | Nocturnal hypoventilation treated with bi-level ventilation | 15 | Moderate | Moderate ID |
| 12 | 14 | | Daytime somnolence | Normal<br>MSLT – 4 naps, 1 sleep, no REM, mean latency 16.6 min | 16 | Moderate | Moderate ID |
| 13 | 15 | Vitamin D | Snoring | REM Hypoventilation | 1 | None | Mild ID |
| 14 | 15 | Vitamin D | Titration study for nocturnal bi-level ventilation | Nocturnal hypoventilation treated with bi-level ventilation | 5 | Moderate | Moderate ID |
| 15 | 15 | Methylphenidate | | | 7 | Mild | Mild ID |
| 16 | 15 | | Daytime somnolence | Early REM hypoventilation<br>MSLT – 4 naps, 1 sleep, no REM, mean latency 18.5 min | 22 | Moderate | Moderate ID |
| 17 | 18 | | | | 5 | Mild | Mild ID |

EDS – excessive daytime sleepiness; ID – intellectual disability; MSLT – Multiple sleep latency test performed following previous night's polysomnography (PSG); PLM – periodic limb movements. PSGs were scored according to 2007 AASM Manual for the Scoring of Sleep and Associated Events [21]; methylphenidate prescribed for attention deficit hyperactivity disorder on school days only.