Sleep Medicine 30 (2017) 160–163

Contents lists available at ScienceDirect

Sleep Medicine

journal homepage: www.elsevier.com/locate/sleep

Original Article

Sleep disorders in spinal muscular atrophy

Maria C. Pera [a, b], Domenico M. Romeo [a], Alessandra Graziano [a, b], Concetta Palermo [a, b], Sonia Messina [c], Giovanni Baranello [d], Giorgia Coratti [a, b], Maria Massaro [a, b], Serena Sivo [a, b], Maria Teresa Arnoldi [d], Elena S. Mazzone [a, b], Laura Antonaci [a, b], Leonardo Lapenta [a, b], Emilio Albamonte [a, b], Lavinia Fanelli [a, b], Roberto de Sanctis [a, b], Gian Luca Vita [c], Maria Sframeli [c], Marika Pane [a, b], Eugenio Mercuri [a, b, *]

[a] Department of Paediatric Neurology, Catholic University, Rome, Italy
[b] Nemo Roma Center for Neuromuscular Disorders, Rome, Italy
[c] Department of Neurosciences and Nemo and Clinical Center, Psychiatry and Anaesthesiology, University of Messina, Messina, Italy
[d] Developmental Neurology Unit, Istituto Neurologico "Besta", Milan, Italy

ARTICLE INFO

Article history:
Received 5 August 2016
Received in revised form
10 November 2016
Accepted 11 November 2016
Available online 30 November 2016

Keywords:
Spinal muscular atrophy
Sleep
Motor function
HFMSE
SDSC

ABSTRACT

Objective: To estimate the frequency of sleep disorders in young persons with type 2 and type 3 spinal muscular atrophy (SMA), and to evaluate the relationship between sleep disorders and different variables such as motor impairment, age, use of ventilation, and use of night orthoses.
Methods: A total of 85 young persons (6–25 years of age) with type 2 and type 3 SMA were assessed using the Sleep Disturbance Scale for Children (SDSC), a scale assessing different sleep factors, and the Hammersmith Functional Motor Scale Expanded (HFMSE), a scale evaluating motor impairment.
Results: An abnormal total sleep score was found in 16.4% of children with SMA; an additional 16.7% had an abnormal score on at least one of the sleep factors assessed by the SDSC. No specific correlation was observed between sleep disturbances and functional level as expressed by the SDSC and total HFMSE scores, but the relationship with individual items on the scale was different. The SDSC total score was significantly associated with the ability to half roll on both sides and to roll from prone to supine on the HMFSE.
Conclusion: Our results demonstrate that sleep disorders are common in children with SMA.

1. Introduction

Spinal muscular atrophy (SMA) is an autosomal recessive disorder characterized by degeneration of the motoneurons in the anterior horn cells due to mutations in the SMN gene located on chromosome 5 (5q11.2–q13.3). This includes heterogeneous clinical groups classified, in the pediatric age group, into three phenotypes on the basis of age of onset and maximum motor function achieved [1]. Type 1 SMA has an onset within six months of age, and infants do not achieve the ability to sit independently. Type 2 has onset between six and 18 months: patients achieve sitting but never walk independently. Type 3 has later onset, and patients achieve the ability to walk independently.

Over the past few years, there has been increasing attention given to possible sleep disorders in SMA. Some studies have reported sleep apneas and other sleep breathing disorders [2,3], whereas others have focused mainly on sleep architecture or specific disturbances detected by polysomnography [3–10]. In type 1 SMA patients, the presence of abnormal sleep microstructure suggested a reduced arousability during non–rapid eye movement (NREM) sleep [7]. Another study in seven SMA children (six with SMA type 1 and one with type 2) also showed impaired sleep architecture that improved with the use of nocturnal noninvasive ventilation (NIV) [8]. An increase of stage 1 sleep, coupled with a decrease or absence of rapid eye movement (REM) sleep, was reported in four patients with an unspecified form of SMA who were part of a larger cohort of 32 neuromuscular patients [9].

Abnormalities of sleep architecture with decreased arousability [10] were also found in a cohort of 17 patients with type 2 SMA.

Recently, it has been suggested that useful information on sleep behavior can also be obtained using questionnaires assessing

* Corresponding author. Pediatric Neurology, Policlinico Gemelli, Largo Gemelli, 00168, Rome, Italy. Fax: +39 06 30154363.
E-mail address: mercuri@rm.unicatt.it (E. Mercuri).

http://dx.doi.org/10.1016/j.sleep.2016.11.012
1389-9457/

several aspects of behavior and sleep quality [11]. The advantage of using a questionnaire is that it can be easily distributed to all families attending the outpatient clinic and can therefore be correlated with other aspects of function measured routinely in SMA patients.

In this study, we used the Sleep Disturbance Scale for Children (SDSC) questionnaire in a multicentric setting, to obtain a large cohort of type 2 and type 3 SMA patients. More specifically, we wished to establish (1) the spectrum of possible sleep disturbances in relation to normative data and an age-matched control group, (2) to correlate the results of the questionnaire with aspects of care such as the use of night orthoses or night ventilation that may interfere with sleep patterns, and (3) to correlate the results of the questionnaire with functional motor scales routinely used in our centers.

2. Methods

The study was performed as part of a multicenter natural history study of SMA patients regularly followed at the Child Neurology Unit/Nemo Center of the Catholic University of Rome, at the Neurological Institute Besta in Milan, and at the Nemo Centre/Neurology Institute in Messina, between January 2013 and December 2015. Enrolled patients had a genetically confirmed diagnosis of SMA with a homozygous deletion of exon7 in the SMN1 gene, and symptom onset after six months, to exclude individuals with type 1 SMA. The questionnaire was used routinely in all type 2 and 3 SMA patients seen in the neuromuscular clinics. As the questionnaire used was originally validated for patients from the age of six years, we included only those patients who were at least six years of age, up to 25 years of age. To have a homogeneous cohort, in the analysis of the study we only included individuals living with their parents, with no parental history of a severe or chronic medical condition (eg, stroke, diabetes) or psychological disorders. The study was approved by the Ethical Committees of all the participating centers (Child Neurology Unit/Nemo Center of the Catholic University of Rome, the Neurological Institute Besta in Milan and Nemo Centre/Neurology Institute in Messina).

Patients were subdivided according to functional status into ambulatory and nonambulatory, the latter including both patients with type 2 and type 3 SMA who lost the ability to ambulate.

2.1. Assessment of sleep disorders

The primary caregiver completed the SDSC [12]. The scale was originally validated on a sample of 1157 healthy children from the general population, aged 6–16 years. It investigates the occurrence of sleep disorders in the six months previous to assessment, and comprises 26 items in a Likert-type scale with scores one to five (higher numerical values reflect a higher clinical severity of symptoms).

The original factor analysis yielded six sleep disturbance factors representing the most common areas of sleep disorders in childhood and adolescence: (1) disorders of initiating and maintaining sleep (DIMS), (2) sleep breathing disorders (SBD), (3) disorders of arousal (sleepwalking, sleep terrors, nightmares) (DA), (4) sleep–wake transition disorders (hypnic jerks, rhythmic movement disorders, hypnagogic hallucinations, nocturnal hyperkinesias, bruxism) (SWTD), (5) disorders of excessive somnolence (DOES), and (6) sleep hyperhidrosis (SHY).

The sum of raw scores can provide both a subscore for each factor and a total raw sleep score with a possible range from 26 to 130. A table, based on normative data, converts the raw scores of the individual factors and the total scores into T scores. A T score of more than 70 (>95th percentile) was regarded as abnormal.

This questionnaire was distributed to the children's primary caregiver during our unit's routine neurological assessment.

As part of our clinical routine, all the patients undergo a functional motor assessment using the Hammersmith Functional Motor Scale Expanded (HFMSE). The scale consists of 33 items, designed to assess motor function in patients with SMA type 2 and type 3, investigating the child's ability to perform various activities. The items range from the ability to sit unsupported and lift the arms to walking and to descend four stairs without a railing.

Each activity (item) is scored on a three-point scoring system, with a score of two for unaided, one for assistance, and zero for inability. A total HFMSE score can be achieved by summing the scores from all individual items. The total score can range from zero, if all the activities are failed, to 66, if all the activities are achieved.

Clinical information on several aspects of care and management including use of orthoses, and nighttime ventilation were duly noted. Aspects of sleep hygiene, such as bed sharing with parents, were also noted.

The study protocol was approved by the ethics committee of the institutions, and informed consent was obtained from the parents.

2.2. Statistical analysis

A *t* test and Pearson product–moment correlation coefficient were used to analyze data. The level of significance was set at 0.05.

The SDSC findings were correlated with a number of variables including age, presence of ventilation, use of night splints, and functional levels expressed by the HFMSE scores. As families report that one of the key elements in nighttime care is related to whether their children can roll or even half roll independently in bed, reducing the number of overnight calls to change position, we specifically compared the SDSC findings to the items of the HFMSE assessing rolling (items 5–9).

3. Results

All carers/caregivers of the 85 patients older than six years (50 male, 35 female) who were given the questionnaire filled out the form, with no refusals. Table 1 shows details of the cohort.

There were no exclusions, as all the patients were living with the parents and there was no parental history of a severe or chronic medical condition (eg, stroke, diabetes) or psychological disorders. HFMSE was administered to all 85 patients. The age of the patients ranged between six and 25 years.

In all, 75 were nonambulatory (70 type 2 and 5 type 3, who lost the ability to ambulate), and 10 were ambulatory (type 3). A total of 22 patients wore night splints, and 17 used night-time ventilation.

3.1. SDSC results

Fourteen children with SMA (16.4%) had an abnormal total sleep T score (>70).

Approximately 34.1% had an abnormal score on at least one of the following SDSC factors: (1) disorders of initiating and maintaining sleep (DIMS), with T scores ranging between 41 and 100, and 13 having abnormal scores (15.3%), (2) sleep breathing disorders (SBD), with scores ranging between 45 and 93, and 15 having abnormal scores (17.6%), (3) disorders of arousal (sleepwalking, sleep terrors, nightmares) (DA), with scores ranging between 35 and 100, and two having abnormal scores (2.3%), (4) sleep–wake transition disorders (SWTD), with scores ranging between 41 and 100, and three having abnormal scores (3.5%), (5) disorders of excessive somnolence (DOES), with scores ranging between 42 and 92, and 10 having abnormal scores (11.7%), and (6) sleep hyperhidrosis (SHY), with scores ranging between 45 and 92, and six having abnormal scores (8.2%).