Clinical Neurophysiology xxx (2013) xxx–xxx

Contents lists available at SciVerse ScienceDirect

Clinical Neurophysiology

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

Sleep disordered breathing in a cohort of patients with sporadic inclusion body myositis

Giacomo Della Marca [a,*], Cristina Sancricca [a], Anna Losurdo [a], Chiara Di Blasi [a], Chiara De Fino [a], Roberta Morosetti [a], Aldobrando Broccolini [a], Elisa Testani [a], Emanuele Scarano [b], Serenella Servidei [a], Massimiliano Mirabella [a]

[a] Institute of Neurology, Catholic University, Rome, Italy
[b] Institute of Otorhinolaryngology, Catholic University, Rome, Italy

ARTICLE INFO

Article history:
Accepted 9 March 2013
Available online xxxx

Keywords:
Sporadic inclusion-body myositis
Sleep
Sleep apnea
Sleep disordered breathing
Polysomnography
Dysphagia

HIGHLIGHTS

- Sporadic inclusion-body myositis (IBM) is the most common muscle disease in the elderly.
- There are no studies addressing sleep disturbances in IBM.
- Our data suggest that poor sleep and sleep disordered breathing are very common in IBM.

ABSTRACT

Objective: The aims of the study were: (1) to evaluate subjective sleep quality and daytime sleepiness in patients affected by sporadic inclusion-body myositis (IBM); (2) to define the sleep and sleep-related respiratory pattern in IBM patients.
Methods: Thirteen consecutive adult patients affected by definite IBM were enrolled, six women and seven men, mean age 66.2 ± 11.1 years (range: 50–80). Diagnosis was based on clinical and muscle biopsy studies. All patients underwent subjective sleep evaluation (Pittsburgh Sleep Quality Index, PSQI and Epworth Sleepiness Scale, ESS), oro-pharingo-esophageal scintigraphy, pulmonary function tests, psychometric measures, anatomic evaluation of upper airways, and laboratory-based polysomnography. Findings in IBM patients were compared to those obtained from a control group of 25 healthy subjects (13 men and 12 women, mean age 61.9 ± 8.6 years).
Results: Disease duration was >10 years in all. Mean IBM severity score was 28.8 ± 5.4 (range 18–36). Dysphagia was present in 10 patients. Nine patients had PSQI scores $\geqslant$ 5; patients had higher mean PSQI score (IBM: 7.2 ± 4.7, Controls: 2.76 ± 1.45, $p = 0.005$); one patient (and no controls) had EES > 9. Polysomnography showed that IBM patients, compared to controls, had lower sleep efficiency (IBM: 78.8 ± 12.0%, Controls: 94.0 ± 4.5%, $p < 0.001$), more awakenings (IBM: 11.9 ± 11.0, Controls: 5.2 ± 7.5, $p = 0.009$) and increased nocturnal time awake (IBM: 121.2 ± 82.0 min., Controls: 46.12 ± 28.8 min., $p = 0.001$). Seven Patients (and no controls) had polysomnographic findings consistent with sleep disordered breathing (SDB).
Conclusion: Data suggest that sleep disruption, and in particular SDB, might be highly prevalent in IBM.
Significance: Data indicate that IBM patients have poor sleep and high prevalence of SDB.

1. Introduction

Sporadic inclusion-body myositis (IBM) is the most common muscle disease of elderly population and presents with slowly progressive atrophy and weakness affecting proximal and distal limb muscles and frequently also pharyngeal and facial muscles (Engel and Askanas, 2006; Needham and Mastaglia, 2007). The disorder has a chronic progressive course, leading to muscle weakness and wasting, that result in severe disability with loss of autonomous deambulation and often severe dysphagia (Engel and Askanas, 2006; Needham and Mastaglia, 2007). Although respiratory muscles are considered to be relatively spared, respiratory impairment has been observed also in IBM patients: pulmonary complications include aspiration pneumonia, interstitial pneumonitis, or respiratory muscle myositis (Teixeira et al., 2005).

* Corresponding author. Address: Department of Neurosciences, Catholic University, Rome, Italy, Policlinico Universitario "A. Gemelli" L.go A. Gemelli, 8 – 00168 Rome, Italy. Tel.: +39 06 30156385; fax: +39 06 35501909.
E-mail address: dellamarca@rm.unicatt.it (G. Della Marca).

1388-2457/$36.00 © 2013 International Federation of Clinical Neurophysiology. Published by Elsevier Ireland Ltd. All rights reserved.
http://dx.doi.org/10.1016/j.clinph.2013.03.002

Sleep abnormalities, in particular poor sleep quality and excessive daytime sleepiness, are common in muscular diseases. Sleep quality impairment and daytime somnolence in these diseases are often secondary to sleep disordered breathing (SDB). SDB is highly prevalent in muscular disorders (Coccagna et al., 1982; Dhand and Dhand, 2006; Dohna-Schwake et al., 2004; Gozal, 2000; Guilleminault et al., 1992). SDB may consist in central alveolar hypoventilation (Coccagna et al., 1982; Dhand and Dhand, 2006; Gozal, 2000; Guilleminault et al., 1992; Sivak et al., 1999), upper airways obstruction due to pharyngeal muscles weakness (Coccagna et al., 1982; Dhand and Dhand, 2006), or thoracic restrictive pathology due to kyphoscoliosis (Dhand and Dhand, 2006; Gozal, 2000). A search of the PubMed Medline, using 'Inclusion Body Myositis' and 'Sleep' as key words, has not revealed any study addressing the issue of sleep disturbances in IBM.

The aims of the present study were: (1) to evaluate sleep quality and daytime sleepiness in a population of patients affected by IBM; (2) to define the sleep pattern and the sleep-related respiratory pattern in IBM patients by means of nocturnal polysomnography; (3) to evaluate the correlations between clinical features and polysomnographic findings. For this reason, we compared subjective sleep measures and polysomnographic findings in a cohort of IBM patients with those obtained from a control group of healthy volunteers.

2. Methods

2.1. Patients

A cohort of 13 consecutive adult patients affected by sporadic IBM were enrolled, six women and seven men, mean age was 66.2 ± 11.1 years (range: 50–80 years). Patients were recruited from the Center for neuromuscular diseases of Catholic University in Rome in a period of eighteen months (from June 2011 to December 2012). The only inclusion criteria was a diagnosis of definite sporadic IBM. Diagnosis of definite IBM in all the patients was based, according to the established criteria (Benveniste and Hilton-Jones, 2009; Griggs et al., 1995), on clinical and muscle biopsy studies. Muscle strength was evaluated by using the Manual Muscle Testing (MMT) and a score was assigned according to the Medical Research Council Scale (MRC (1976)). MMT score ranges from 0 = "no movement, no visible or palpable contraction" to 5 = "segment movement through full range of motion against gravity and ability to hold against resistance". In order to measure the clinical severity of the disease, the IBM Functional Rating Scale (IBM-FRS) (Jackson et al., 2008) was applied. In order to evaluate the effects of anxiety and depression, a psychometric evaluation was performed, which included the Self-Administered Anxiety Scale (SAS #54) (Zung, 1971) and the Beck's Depression Inventory (BDI) (Beck et al., 1961). The SAS #54 (Zung, 1971) is a method of measuring levels of anxiety in patients who have anxiety-related symptoms. It uses a 4-point Likert-type scale, ranging from 1 to 4. The SAS contains 20 items with 15 increasing anxiety level questions and 5 items reverse scored. The total score ranges from 20 to 80; the normal range is 20 to 44. The BDI (Beck et al., 1961) is a 21-item well-validated self-report instrument measuring characteristic attitudes and symptoms of depression over the previous two weeks. Scores range from 0 to 36; scores > 9 indicate mild to severe depression. Clinical and polysomnographic (PSG) data in patients were compared with those obtained in a control group of healthy volunteers.

2.2. Controls

Clinical and polysomnographic data obtained in patients were compared with data recorded in a control group of 25 healthy subjects matched for age and gender (13 men and 12 women, mean age 61.9 ± 8.6); this population of healthy volunteers was previously enrolled for the specific purpose to serve as control subjects for sleep studies. The sleep study, in the control group, included the evaluation of sleep quality by means of the PSQI and of ESS, and the administration of the scales for anxiety (SAS#54) and depression (BDI). Polysomnographies in Controls were performed in the same setting and with same technique applied to patients; also the scoring of PSG tracings was performed with the same criteria used for patients, and by the same scorers. All patients and controls were fully informed and all gave a written consent to participate in the study. The study was performed in agreement with the Declaration of Helsinki and was approved by Ethics Committee of the Catholic University in Rome.

2.3. Sleep quality evaluation

Subjective evaluation of sleep quality was performed by means of the Pittsburgh Sleep Quality Index (PSQI). The validated Italian version was used (Curcio et al., 2012). A global score $\geqslant 5$ was considered as an indicator of poor sleep quality. For the evaluation of excessive daytime sleepiness (EDS), the validated Italian version of the Epworth Sleepiness Scale (ESS) (Vignatelli et al., 2003) was applied. Moreover, in all subjects an evaluation of the symptoms and clinical signs predictors of OSAS was performed by means of the Berlin's Questionnaire (Netzer et al., 1999). Neck circumference and Body Mass Index (BMI) were measured in all patients.

2.4. Polysomnography

Full-night, laboratory-based polysomnographies were recorded in acclimatized, sound-proof rooms, following adaptation. Recording montage included EEG leads filled with electrolyte applied to following locations: Fp1, Fp2, C3, C4, T3, T4, O1, O2; reference electrodes applied to the left (A1) and right (A2) mastoids; 2 EOG electrodes applied to the outer ocular cantus and referred to the contra-lateral mastoid, surface EMG of sub-mental and intercostal muscles, airflow measured by nasal-cannula pressure transducers, thoracic and abdominal effort, EKG and peripheral hemoglobin saturation measured by a clip sensor placed on a finger or on the earlobe. Continuous audio and video recording was performed by means of infra-red cameras. Sleep recordings were analyzed on computer monitor, and sleep stages were visually classified according to the criteria of the American Academy of Sleep Medicine (AASM, 2007) (Iber et al., 2007). The arousal indexes (number of arousals per hour) were calculated for total sleep, NREM and REM stages.

The scoring of sleep-related respiratory events was performed according to the criteria established by the AASM (2007) (Iber et al., 2007). The analysis of the SpO_2 parameters was made with a dedicated software (Rembrandt SleepView-Medcare®). Oxygen desaturation events were scored when a fall in $SpO_2 \geqslant 4\%$ was observed. The parameters considered were: baseline SpO_2, lowest SpO_2, Oxygen Desaturation Indexes (ODI) in total sleep, in NREM and in REM.

Snoring was quantified according to a 4 point score: − (no snoring), + (snoring occurring in Slow Wave Sleep or REM *and* in supine position), ++ (snoring occurring in Slow Wave Sleep or REM, regardless of the position, *or* in supine position, regardless of the sleep stage), +++ (snoring occurring in all positions and in all sleep stages). Obstructive Sleep Apnea syndrome (OSAS) was defined by the presence of an Apnea–Hypopnea Index (AHI) >5 events per hour of sleep (including obstructive and mixed events); Central Sleep Apnea syndrome (CSAS) was defined by the presence of a Central Apnea–Hypopnea Index (CAHI) >5 events per hour of sleep (including only central events).

In order to evaluate spontaneous motility during sleep, which is a possible mechanism of sleep disruption (Della Marca et al., 2011),

we measured Major Body Movements (MBM) during sleep. MBM were defined on the basis of video-polygraphic findings, in accordance with the criteria established by the AASM (Iber et al., 2007). MBM were defined, on the PSG tracings, as movements obscuring the EEG for more than half an epoch. The occurrence of a MBM was verified on the video recordings. A MBM index was calculated, defined as the number of MBM per hour of sleep.

2.5. Anatomic evaluation of upper airways

A detailed evaluation of upper airways anatomy was performed in all patients. Otorhinolaryngologic evaluation was aimed at measuring the morphology of upper airways and identifying potential sites of collapse. The main parameters considered were Mallampati score (Mallampati et al., 1985) and Fujita's class (presence of palatal or pharyngeal narrowing) (Fujita et al., 1991). Optical fibers pharyngo-laryngoscopy was performed.

2.6. Dysphagia evaluation

All Patients were further investigated by means of oro-pharingo-esophageal scintigraphy (OPES). OPES provides information on the swallowing phases. It is based on the rapid sequential acquisition of 480 images after the administration of 10 ml of water containing 37 MBq of ^{99}mTc-colloid. The evaluation of sequential scintigraphic images and the activity/time curves allows qualitative and quantitative analysis of swallowing disorders. The main qualitative parameters are the following: bolus fragmentation with multiple swallowing, naso-pharyngeal or pharyngo-oral refluxes, premature ingestion of the bolus, laryngo-tracheal aspiration. For a detailed definition of the OPES parameters, see: Shaw et al., 2004 (Shaw et al., 2004).

2.7. Pulmonary function test

All patients performed diagnostic pulmonary function tests (PFT), that included the measures of Vital Capacity (VC), Forced Vital Capacity (FVC), Maximal Inspiratory Pressure (MIP), Maximal Expiratory Pressure (MEP) and blood gas analysis.

2.8. Statistical analysis

Clinical and PSG data were compared between IBM patients and Controls and, within the IBM patients group, between patients with and without SDB. The results of this latter comparison might be biased by the low number of patients in the IBM group. A non-parametric Mann–Whitney *U*-test was used for comparing numerical variables, whereas the Fisher's Exact test was used for categorical values (i.e. presence versus absence of dysphagia; normal versus abnormal PSG respiratory indexes). In case of multiples comparison, in order to avoid family-wise type-I errors, a formal Bonferroni correction was applied to each family of comparisons, by dividing the limit of significance by the number of comparisons. Statistics were performed using the SYSTAT 12 software, version 12.02.00 for Windows® (copyright SYSTAT® Software Inc. 2007).

3. Results

3.1. Clinical measures

All patients fulfilled the diagnostic criteria for IBM. Disease duration was >10 years in all patients. Mean severity score (IBM-FRS) was 28.8 ± 5.4 (range 18–36). Dysphagia was present in 10 patients, in eight cases due to oro-pharyngeal dysfunction. Psychometric measure revealed normal level of anxiety in all patients (mean SAS#54 score: 36.8 ± 5.6; no patient was above the cut-off value = 44); nevertheless, the mean SAS#54 score was higher in patients than in controls (IBM: 36.7 ± 5.6, Controls: 31.0 ± 5.9, *U*-test = 62.0, $p = 0.002$). Two patients had a mild mood disturbance (mean BDI score 4.4 ± 3.8, cut-off value = 10); the BDI did not differ between patients and Controls (IBM: 4.4 ± 3.8, Controls: 2.8 ± 1.7, *U*-test = 126.5, $p = 0.263$). Detailed clinical and morphological data of the population are reported in Table 1. No significant differences were observed between patients and controls in age, gender, BMI, neck's circumference. Results of comparison between patients and controls are reported in Table 2.

3.2. Subjective sleep evaluation

Mean PSQI was 7.2 ± 4.7; nine patients had PSQI above the cut-off value for poor sleep; as compared to Controls, IBM patients had higher PSQI scores (IBM: 7.2 ± 4.7, Controls: 2.76 ± 1.45, *U*-test = 72.5, $p = 0.005$). Mean ESS was 5.9 ± 6.1; only one patient had ESS above the cut-off value for excessive daytime sleepiness; no significant differences were observed between patients and Controls (IBM: 5.9 ± 6.1, Controls: 3.0 ± 2.2, *U*-test = 109.0, $p = 0.097$). Mean Berlin score was 0.4 ± 0.5; five patients had a score above the cut-off value for sleep apnea. Mean BMI was 25.5 ± 3.9 kg/m^2; mean neck circumference was 37.0 ± 4.1 cm; one patient had BMI above the cut-off value for the risk of OSAS, three patient had neck circumference above the cut-off value for the risk of OSAS, no patient had both the parameters above the cut-off. Results of the subjective sleep evaluation are reported in Table 1. Results of comparison between patients and controls are reported in Table 2.

3.3. Polysomnography

Useful PSG recordings were obtained in 12 out of 13 patients: in one patient (patient #11) the sleep period recorded during polysomnography was extremely short (<60 min) and no epoch of REM sleep was scored; for this reason, a reliable evaluation of the respiratory parameters was not possible in this patient. In another patient (patient #5) the analysis of respiratory pattern during sleep was limited by the presence of tracheostomy. In this patient #5, tracheotomy was performed, one year before the present study, because of recurrent episodes of aspiration pneumonia, caused by severe dysphagia.

As compared to controls, IBM patients showed several differences in PSG indexes suggesting disrupted sleep: sleep latency was slightly increased in IBM patients, though it did not reach statistical significance (IBM: 34.4 ± 44.5 min., Controls: 18.3 ± 11.9 min., *U*-test = 184.5, $p = 0.498$); mean sleep efficiency index (SEI) was markedly reduced (IBM: 78.8 ± 12.0%, Controls: 94.0 ± 4.5%, *U*-test = 301.0, $p < 0.001$), mean duration of wakefulness after sleep onset (WASO) was increased (IBM: 121.2 ± 82.0 min., Controls: 46.12 ± 28.8 min., *U*-test = 52.5; $p = 0.001$); the mean number of awakenings lasting more than one minute was higher (IBM: 11.9 ± 11.0, Controls: 5.2 ± 7.5, *U*-test = 78.0, $p = 0.009$). No significant differences were observed, between the groups, in the arousal indexes.

On the basis of the scoring of respiratory events in PSG, the patients were classified into 2 subgroups: patients without SDB (SDB–) and patients with SDB (SDB+). SDB was detected in 7 out of 12 patients (58.3%). Three patients had purely obstructive, one patient had purely central SDB (patient #5, who underwent tracheostomy three years before the present study) and two patients had both central and obstructive events. SDB was of moderate entity in most patients; five patients showed obstructive AHI > 15 events/hour. The mean number of MBM in IBM patients was 19.5 ± 12.3 events per night, corresponding to a MBM index of 5.3 ± 8.0

Table 1
Demographic and clinical data. Demographic and clinical data of IBM patients. BMI, Body Mass Index (kg/m^2); Neck, neck circumference (cm); IBM-FRS, IBM Functional Rating Scale; OPES, oro-pharingo-esophageal scintigraphy; PFT, Pulmonary Function Tests; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; Berlin, Berlin's Questionnaire; SAS, Self-Administered Anxiety Scale; BDI, Beck's Depression Inventory; n.a., not applicable.

Patients	Age (years)	Gender	BMI (kg/m^2)	Neck (cm)	IBM-FRS	Dysphagia	OPES	PFT	PSQI	ESS	Berlin	SAS	BDI
1	77	M	26.0	40.0	33	Yes	Oro-pharyngeal	Mild restrictive	6	6	0	41	6
2	50	M	34.6	41.0	27	No	n.a.	Mild restrictive	7	11	1	38	11
3	78	M	26.4	38.0	18	Yes	Normal	Normal	1	2	0	35	2
4	72	F	22.9	34.0	24	Yes	Oro-pharyngeal	Normal	6	4	0	36	2
5	51	M	25.6	35.0	30	Yes	Oro-pharyngeal	Severe obstructive	2	2	0	35	6
6	53	F	27.8	33.0	35	No	n.a.	Normal	1	24	0	36	0
7	65	F	21.9	30.0	29	Yes	Oro-pharyngeal	Mild restrictive	7	1	0	20	0
8	75	M	24.0	40.0	21	No	n.a.	Normal	13	3	0	42	6
9	73	M	24.5	38.0	27	Yes	Normal	Mild obstructive	12	6	1	43	11
10	52	F	26.8	42.0	32	Yes	Oro-pharyngeal	Mild obstructive	3	7	0	37	1
11	65	F	17.6	30.5	34	Yes	Oro-pharyngeal	Severe restrictive	15	3	1	38	5
12	80	M	27.3	42.0	36	Yes	Oro-pharyngeal	Normal	12	6	1	38	6
13	70	F	25,71	37.0	28	Yes	Oro-pharyngeal	Normal	9	2	1	39	1
Mean	66.2		25.5	37.0	28.8				7.2	5.9	0.4	36.8	4.4
S.D.	11.1		4.0	4.1	5.4				4.7	6.1	0.5	5.6	3.8

Table 2
Comparison of clinical and PSG data between the IBM group and the control group. n = number of patients in the sample; SD = standard deviation; n.a., not applicable; BMI, Body Mass Index (kg/m^2); Neck, neck circumference (cm); PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; SAS#54, Self-Administered Anxiety Scale; BDI, Beck's Depression Inventory; TST, Total Sleep Time; SEI, Sleep Efficiency Index; WASO, Wake After Sleep Onset; Awakenings >1 min; O_AHI, obstructive apnea–hypopnea index; C_AHI, central apnea–hypopnea index; ODI, oxygen desaturation index.

	IBM (n = 13)		Controls (n = 25)		Mann–Whitney		Fisher's exact test
	Mean	SD	Mean	SD	U-test	p	p
Clinical results							
BMI	25.28	4.19	24.32	1.42	153.0	0.875	
Neck	36.96	4.15	37.36	1.87	159.5	0.926	
Dysphagia	10+, 3-		0+, 25-				<0,001
PSQI	7.23	4.73	2.76	1.45	72.5	0.005	
ESS	5.92	6.09	3.04	2.23	109.0	0.097	
SAS#54	36.77	5.64	31.04	5.92	62.0	0.002	
BDI	4.38	3.78	2.76	1.64	126.5	0.263	
PSG scores							
TST	358.50	131.14	401.74	44.70	194.5	0.325	
Sleep latency	34.38	44.49	18.26	11.89	184.5	0.498	
SEI	78.79	12.04	94.03	4.48	301.0	<0,001	
REM/TST	16.25	8.27	17.66	7.64	163.0	0.988	
N1	11.15	7.36	11.03	9.26	153.5	0.782	
N2	52.08	12.89	40.43	12.81	86.0	0.019	
N3	17.22	10.15	20.70	11.24	193.0	0.348	
WASO	121.23	82.05	46.14	28.80	52.5	0.001	
Awakenings	11.92	11.00	5.20	2.75	78.0	0.009	
Major body movements	3.18	2.29	3.19	1.19	174.0	0.723	
Arousal index	13.16	4.23	8.65	7.54	229.0	0.040	
Arousal NREM	13.28	4.46	8.66	7.66	229.0	0.040	
Arousal REM	12.76	4.77	8.43	8.65	233.0	0.030	
O_AHI	10.01	11.33	2.11	1.52			<0,001
C_AHI	1.99	2.99	0.60	0.47			0.009
ODI	14.48	23.20	2.64	1.40			0.002

events/hour of sleep; this score was not significantly different in IBM patients and Controls. Results of the scoring of polysomnograms and indexes of sleep-related respiratory events and MBM are reported in Tables 3 and 4. None of the subjects in the Control group showed PSG scores consistent with SDB. Obstructive AHI was abnormal in 6/12 patients and in 0/25 controls ($p < 0.001$); Central AHI was abnormal in 3/12 patients and in 0/25 controls ($p = 0.009$); ODI was abnormal in 4/12 patients and in 0/25 controls ($p = 0.002$). In the comparison, within IBM group, between patients with SDB (SDB+, $n = 7$) and patients without SDB (SDB−, $n = 5$) the only significant difference was found in neck's circumference (SDB+ 39.7±2.5 cm, SDB− 34.4±3.2 cm). No significant differences were found in sleep structure between the two groups. Also the MBM index, a measure of nocturnal motility, did not show significant differences between patients and controls.Detailed results of the comparison between patients and controls are listed in Table 2; results of the comparison between IBM SDB+/SDB− patients are listed in Table 5.

3.4. ORL evaluation

One patient did not underwent upper airway evaluation because of the presence of tracheotomy. Hypertrophic tonsils were observed in two patients, hypertrophic uvula in three, hypotonic soft palate in five, macroglossia in five. Hypotrophic tonsils were detected in two patients, hypotrophic uvula in one patient. One patient had tongue hemyatrophy. Results of the ORL evaluation are reported in Table 6.

4. Discussion

The present study reports the results of a clinical and polysomnographic observation in a cohort of patients affected by sporadic

Table 3
Polysomnographic results. Polysomnographic results: TIB, Time In Bed; TST, Total Sleep Time; SPT, Sleep Period Time; SEI, Sleep Efficiency Index; WASO, Wake After Sleep Onset; Awakenings >1 min, number of awakenings lasting longer than 1 min.

Patients	TIB (min)	TST (min)	SPT (min)	Sleep latency (min)	SEI (%)	REM latency (min)	REM (%)	N1 (%)	N2 (%)	N3 (%)	WASO (min)	Awakenings >1 min
1	485	362	446	16	81.3	83.5	6.6	16.2	52.4	24.9	107.0	14
2	518	282	406	111	67.2	331.0	10.6	26.2	62.9	0.2	134.5	45
3	610	514	600	9	85.7	126.5	9.8	7.6	73.7	8.9	87.0	10
4	524	358	506	16	70.5	93.5	14.7	8.0	49.1	28.3	151.0	16
5	534	490	526	6	93.1	75.5	23.9	4.3	53.4	18.4	38.5	3
6	400	364	395	5	92.0	43.0	23.6	2.1	61.4	12.9	31.5	2
7	350	188	271	76	68.8	181.0	14.6	8.8	40.4	36.2	87.5	8
8	587	339	468	69	72.5	94.0	15.9	15.2	57.4	11.5	179.0	16
9	464	405	457	4	88.6	103.0	27.4	7.5	47.5	17.6	55.5	9
10	586	481	528	6	91.0	20.5	22.0	13.5	52.6	12.0	100.0	12
11	503	46	76	126	60.0	n.a.	0.0	7.9	23.7	25.9	331.5	3
12	564	353	556	6	63.4	25.5	27.0	4.4	63.8	4.8	205.5	6
13	549	481	534	1	90.2	103.5	15.1	23.3	38.7	22.5	67.5	11
Mean	513.0	358.5	443.5	34.4	78.8	115.2	16.3	11.1	52.1	17.2	121.2	11.9
S.D.	75.0	131.1	139.1	44.5	12.0	87.5	8.3	7.4	12.9	10.2	82.0	11.0

Table 4
Respiratory PSG results. Polysomnographic results: C-AHI, Central Apnea–Hypopnea Index; O-AHI, obstructive Apnea–Hypopnea Index; ODI, Oxygen Desaturation Index; PAP, Positive Airway Pressure; n.a., not available; MBM, Major Body Movements; RBM, ratio of MBM (MBM per hour of sleep).

Patients	C_AHI	O_AHI	ODI	Nadir SpO2 (%)	Arousal TST (events/h)	Arousal NREM (events/h)	Arousal REM (events/h)	Snoring	SDB	PAP ventilation	MBM	RBM (events/h)
1	0.8	25.2	46.9	68.8	4.0	4.1	2.5	+++	+	+	9	1.49
2	1.3	29.6	72.8	86.5	11.3	12.4	2.0	+++	+	+	44	9.36
3	0.1	15.6	1.6	85.4	15.6	15.3	19.0	++	+		23	2.68
4	0.0	1.0	2.2	79.4	11.1	12.2	4.6	++	–		19	3.19
5	5.6	n.a.	4.3	83.4	19.1	19.7	17.4	n.a.	+	Tracheotomy	32	3.92
6	0.0	1.2	1.0	86.4	2.0	1.7	2.8	–	–		5	0.82
7	0.0	0.0	4.8	80.5	5.1	5.6	2.2	–	–		11	3.51
8	9.6	17.2	14.3	80.4	24.3	24.4	23.3	–	+	+	15	2.65
9	0.7	0.9	1.1	77.4	1.2	0.8	2.2	++	–		25	3.71
10	5.2	23.7	37.8	77.5	11.9	9.6	19.9	++	+	+	13	1.62
11	0.0	0.0	0.0	0.0	1.3	1.3	n.a.	–			0	0.00
12	2.4	5.3	0.9	89.0	3.4	3.0	4.4	++	+		27	4.60
13	0.1	1.5	0.6	90.0	2.3	2.5	0.8	++			30	30.70
Mean	2.0	10.1	14.5	75.7	8.7	8.7	8.4				19.5	5.3
S.D.	3.0	11.4	23.2	23.5	7.5	7.7	8.6				12.3	8.0

Table 5
Descriptive statistics and statistical comparison in the two groups of IBM patients: with SDB (SDB+) and without SDB (–). *n* = number of patients in the sample; SD = standard deviation; BMI, Body Mass Index (kg/m^2); Neck, neck circumference (cm); IBMQ, IBM Functional Rating Scale; PSQI, Pittsburgh Sleep Quality Index; ESS, Epworth Sleepiness Scale; BerlinSAS, Self-Administered Anxiety Scale; BDI, Beck's Depression Inventory; TST, Total Sleep Time; SEI, Sleep Efficiency Index; WASO, Wake After Sleep Onset; Awakenings >1 min: number of awakenings lasting longer than 1 min. All statistical comparison were performed by means of a non-parametric Mann–Whitney *U*-test; only the presence of Dysphagia (a dicotomical variable) was compared in the groups by means of Fisher's exact test (indicated with a* in the Table).

	SDB+ (n = 7)		SDB– (*n* = 5)		Mann–Whitney	Fisher's exact test
	Mean	SD	Mean	SD	*U*-test	*p*
Clinical results						
BMI	27.23	3.74	24.28	2.58	9.000	0.167
Neck	39.71	2.50	34.40	3.21	2.500	0.014
IBM-Q	28.14	6.57	28.60	4.04	18.500	0.871
Dysphagia	5+ 2–		4+ 1–			0.735
PSQI	6.29	4.75	7.00	4.06	19.000	0.806
ESS	5.29	3.25	7.40	9.48	15.000	0.680
SAS	38.00	2.71	34.80	8.76	16.000	0.807
BDI	5.43	3.26	2.80	4.66	8.500	0.134
PSG scores						
TST	402.79	90.16	359.00	107.50	16.000	0.808
Sleep latency	31.57	41.65	20.10	31.50	11.000	0.290
SEI	79.17	11.67	82.01	11.38	20.000	0.685
REM/TST	16.54	7.86	19.09	6.04	21.000	0.570
N1	12.49	7.83	9.93	7.92	14.000	0.570
N2	59.46	7.90	47.41	9.00	4.000	0.028
N3	11.51	8.23	23.47	9.11	30.000	0.042
WASO	121.64	56.69	78.60	45.27	9.000	0.167
Awakenings	15.14	13.91	9.20	5.07	12.500	0.416
Major body movements	23.29	12.23	18.00	10.15	13.000	0.465

Please cite this article in press as: Della Marca G et al. . Clin Neurophysiol (2013), http://dx.doi.org/10.1016/j.clinph.2013.03.002

Table 6
ORL evaluation. Results of ORL evaluation. n.a.: not available.

Patients	Turbinates hypertrophy	Nasal septum	Adenoids	Tonsils	Macroglossia	Soft palate	Uvula	Mallampati	Fujita's class	Larynx
1	Mild	Italic 'S' deviation	No	Normal	Mild	Hypotonia	Hypertrophy	II	II	Normal
2	Mild	Right deviation	No	Normal	No	Hypotonia	Hypertrophy	II	II	Normal
3	Severe	Right deviation	No	Mild hypertrophy	Mild	Normal	Normal	II	I	Normal
4	Severe	Italic 'S' deviation	No	Hypotrophy	No	Normal	Hypotrophy	II	II	Normal
5	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.	n.a.
6	Severe	Italic 'S' deviation	No	Normal	Mild	Hypotonia	Normal	III	III	Normal
7	Mild	No	No	Normal	No	Normal	Mild hypertrophy	II	II	Normal
8	Moderate	Complex deviation	No	Hypotrophy	No	Hypotonia	Normal	III	II	Vocal chord oedema
9	Severe	Italic 'S' deviation	No	Mild hypertrophy	Mild	Hypotonia	Normal	II	II	Normal
10	Mild	Italic 'S' deviation	No	Normal	Moderate	Normal	Normal	II	II	Normal
11	Mild	Right deviation	No	Normal	No	Normal	Normal	II	I	Vocal cord paresis
12	Severe	S' deviation	No	No	Hemyatrophy	Normal	Normal	II	I	Normal
13	Mild	Normal	No	Normal	No	Normal	Normal	II	I	Normal

IBM. The main objectives of the study were to evaluate sleep quality in IBM, using both subjective and objective measures, and to evaluate the prevalence and the clinical features of SDB.

As concerns sleep quality, poor sleep was reported by most patients (9 out of 13 had a PSQI > 5). Compared to controls, IBM patients had higher scores of PSQI (which indicate poorer sleep quality). All IBM patients had anxiety scores below the cut-off values for anxiety disorders, but their mean score was significantly higher than that of controls. Objective PSG recordings confirmed this data, demonstrating a long sleep latency (in the average, above 30 min) and a reduced sleep efficiency (below 85%). In particular, IBM patients, with respect to controls, had lower sleep efficiency, increased number of awakenings from sleep, and, consequently, increased amount of nocturnal wakefulness. One patient (#11) had an almost total insomnia. Nevertheless, subjective excessive daytime sleepiness, a frequent consequence of poor sleep, was present in only one subject (the one with tracheotomy). Patients and controls did not differ in the mean scores of daytime sleepiness.

Poor sleep quality has been documented in many other neuromuscular disorders, including muscular dystrophies (Dauvilliers and Laberge, 2012; Della Marca et al., 2007; Laberge et al., 2004), amyotrophic lateral sclerosis (Lo Coco and La Bella, 2012), myasthenia gravis (Dhand and Dhand, 2006), and neuropathies (Dhand and Dhand, 2006); in these diseases, sleep disruption is due to a variety of mechanisms, which include depressed mood, reduced motility in bed (Della Marca et al., 2011; Dhand and Dhand, 2006) and respiratory impairment (Dhand and Dhand, 2006). Sleep disturbances may or may be not related to the severity of muscular impairment, and, in general, no clinical predictors of sleep disruption are present in these patients. Due to the small number of patients in our cohort, it was not possible to evaluate statistical correlations between clinical parameters and sleep measures; nevertheless, scores on depression and anxiety scales were substantially normal in all subjects, though patients had anxiety (but not depression) scores slightly higher than controls. Analogously, the analysis of MBM revealed a substantially normal motor pattern in sleep, since MBM indexes in patients and controls did not show significant differences. These data seem to suggest that SDB might be the main pathogenic mechanism of sleep disruption in these patients.

The second endpoint of the study was to assess the respiratory pattern during sleep. IBM is a severe, progressive muscular disease, sometimes associated with respiratory impairment, either primary (Voermans et al., 2004) or secondary to diaphragmatic dysfunction (Cohen et al., 1993); for this reason, it seems necessary to evaluate sleep-related respiratory function in these patients. In our population abnormal respiratory function test were observed in seven patient (four with a restrictive pattern, three with obstructive). SDB was present in seven patients, including one who had undergone tracheotomy prior to the sleep study: four patients had OSAS, one had Central Sleep Apnea and two had both central and obstructive respiratory events. SDB was classified 'moderate' in most cases. Abnormal respiratory indexes, suggesting SDB, were not detected in any of the subjects of the control group. Four patients needed positive airway pressure (PAP) ventilation. Among the patients with OSAS, only one had BMI above the values considered as predictors of OSAS. Only one of the SDB patients had daytime sleepiness (patient #2), patient 6# also hade ESS scores indicating excessive sleepiness, despite normal PSG values and sleep-related respiratory indexes. Berlin's score was = 0 in 8/13 patients. Taken together, these data suggest that in IBM, as well as in other neuromuscular diseases, clinical data are not reliable predictors of SDB (Gozal, 2000).

Dysphagia is frequent in IBM, and it was highly prevalent in our cohort (Oh et al., 2008). Dysphagia was observed in 10 patients of our cohort; the OPES study proved that the pathogenic mechanism was oropharyngeal dysfunction in most cases (8 out of 10). In five patients dysphagia and OSAS coexisted in the same patient. It could be hypothesized that dysphagia and sleep-related airway obstruction may share a common pathogenic mechanism. Sleep-related respiratory obstruction is due to upper airway collapse during sleep, and the segment of airway in which collapse most likely occurs is the pharynx. Consequently, both dysphagia and OSAS can ultimately be caused by a pharyngeal muscular dysfunction. Nevertheless, the result of this study do not allow to prove this hypothesis, since one patient with dysphagia had normal PSG respiratory indexes (AHI < 5events/h), and two patients without dysphagia had pathologic indexes; further studies, enrolling greater number of patients, are needed to confirm or rule out the hypothesis of a pathogenic association between OSAS and dysphagia.

Please cite this article in press as: Della Marca G et al. . Clin Neurophysiol (2013), http://dx.doi.org/10.1016/j.clinph.2013.03.002

4.1. Study limitations

The major limitation of the present study is represented by the small size of the cohort of patients enrolled. This depends essentially on the very low prevalence of IBM in the general population. The small number of patients enrolled, therefore, could bias statistical evaluations, and did not permit to establish defined relations between instrumental findings and clinical data.

5. Conclusions

In conclusion, the present data suggest that sleep disruption, and in particular SDB might be highly prevalent in IBM. An association with the severity of muscular impairment, and in particular with dysphagia, can be hypothesized. These data, obtained from a relatively small sample of patients, suggest that sleep study should be included in the routinary clinical assessment of IBM patients, in particular if dysphagia or respiratory impairment are present.

Disclosure

The Authors have no financial interests and no funding source supporting the work to disclose.

References

Beck AT, Ward CH, Mendelson M, Mock J, Erbaugh J. An inventory for measuring depression. Arch Gen Psychiatry 1961;4:561–71.

Benveniste O, Hilton-Jones D. International Workshop on Inclusion Body Myositis held at the Institute of Myology, Paris, on 29 May 2009. Neuromuscular Disord 2009;20:414–21.

Coccagna G, Martinelli P, Lugaresi E. Sleep and alveolar hypoventilation in myotonic dystrophy. Acta Neurol Belg 1982;82:185–94.

Cohen R, Lipper S, Dantzker DR. Inclusion body myositis as a cause of respiratory failure. Chest 1993;104:975–7.

Curcio G, Tempesta D, Scarlata S, Marzano C, Moroni F, Rossini PM, et al. Validity of the Italian version of the pittsburgh sleep quality index (PSQI). Neurol Sci 2012. http://dx.doi.org/10.1007/s10072-012-1085-y.

Dauvilliers YA, Laberge L. Myotonic dystrophy type 1, daytime sleepiness and REM sleep dysregulation. Sleep Med Rev 2012;16:539–45.

Della Marca G, Frusciante R, Dittoni S, Vollono C, Losurdo A, Testani E, et al. Decreased nocturnal movements in patients with facioscapulohumeral muscular dystrophy. J Clin Sleep Med 2011;6:276–80.

Della Marca G, Frusciante R, Vollono C, Dittoni S, Galluzzi G, Buccarella C, et al. Sleep quality in Facioscapulohumeral muscular dystrophy. J Neurol Sci 2007;263:49–53.

Dhand UK, Dhand R. Sleep disorders in neuromuscular diseases. Curr Opin Pulm Med 2006;12:402–8.

Dohna-Schwake C, Ragette R, Mellies U, Straub V, Teschler H, Voit T. Respiratory function in congenital muscular dystrophy and limb girdle muscular dystrophy 2I. Neurology 2004;62:513–4.

Engel WK, Askanas V. Inclusion-body myositis: clinical, diagnostic, and pathologic aspects. Neurology 2006;66:S20–9.

Fujita S, Woodson BT, Clark JL, Wittig R. Laser midline glossectomy as a treatment for obstructive sleep apnea. Laryngoscope 1991;101:805–9.

Gozal D. Pulmonary manifestations of neuromuscular disease with special reference to Duchenne muscular dystrophy and spinal muscular atrophy. Pediatr Pulmonol 2000;29:141–50.

Griggs RC, Askanas V, DiMauro S, Engel A, Karpati G, Mendell JR, et al. Inclusion body myositis and myopathies. Ann Neurol 1995;38:705–13.

Guilleminault C, Stoohs R, Quera-Salva MA. Sleep-related obstructive and nonobstructive apneas and neurologic disorders. Neurology 1992;42:53–60.

Iber C, Ancoli-Israel S, Chesson A, Quan SF. The AASM manual for scoring of sleep and associated events: rules, terminology and technical specifications. 1st ed. Westchester, IL: American Academy of Sleep Medicine; 2007.

Jackson CE, Barohn RJ, Gronseth G, Pandya S, Herbelin L. Inclusion body myositis functional rating scale: a reliable and valid measure of disease severity. Muscle Nerve 2008;37:473–6.

Laberge L, Begin P, Montplaisir J, Mathieu J. Sleep complaints in patients with myotonic dystrophy. J Sleep Res 2004;13:95–100.

Lo Coco D, La Bella V. Fatigue, sleep, and nocturnal complaints in patients with amyotrophic lateral sclerosis. Eur J Neurol 2012;19:760–3.

Mallampati SR, Gatt SP, Gugino LD, Desai SP, Waraksa B, Freiberger D, et al. A clinical sign to predict difficult tracheal intubation: a prospective study. Can Anaesth Soc J 1985;32:429–34.

Medical Research Council e. Aids to examination of the peripheral nervous system. London: Her Majesty's Stationery Office London; 1976.

Needham M, Mastaglia FL. Inclusion body myositis: current pathogenetic concepts and diagnostic and therapeutic approaches. Lancet Neurol 2007;6:620–31.

Netzer NC, Stoohs RA, Netzer CM, Clark K, Strohl KP. Using the Berlin Questionnaire to identify patients at risk for the sleep apnea syndrome. Ann Intern Med 1999;131:485–91.

Oh TH, Brumfield KA, Hoskin TL, Kasperbauer JL, Basford JR. Dysphagia in inclusion body myositis: clinical features, management, and clinical outcome. Am J Phys Med Rehabil 2008;87:883–9.

Shaw DW, Williams RB, Cook IJ, Wallace KL, Weltman MD, Collins PJ, et al. Oropharyngeal scintigraphy: a reliable technique for the quantitative evaluation of oral-pharyngeal swallowing. Dysphagia 2004;19:36–42.

Sivak ED, Shefner JM, Sexton J. Neuromuscular disease and hypoventilation. Curr Opin Pulm Med 1999;5:355–62.

Teixeira A, Cherin P, Demoule A, Levy-Soussan M, Straus C, Verin E, et al. Diaphragmatic dysfunction in patients with idiopathic inflammatory myopathies. Neuromuscul Disord 2005;15:32–9.

Vignatelli L, Plazzi G, Barbato A, Ferini-Strambi L, Manni R, Pompei F, et al. Italian version of the Epworth sleepiness scale: external validity. Neurol Sci 2003;23:295–300.

Voermans NC, Vaneker M, Hengstman GJ, ter Laak HJ, Zimmerman C, Schelhaas HJ, et al. Primary respiratory failure in inclusion body myositis. Neurology 2004;63:2191–2.

Zung WW. A rating instrument for anxiety disorders. Psychosomatics 1971;12:371–9.