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Nocturnal Sleep and Oxygen Balance in Duchenne Muscular Dystrophy

A Clinical and Polygraphic 2-year Follow-up Study

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Summary. A long-term, clinical and polygraphic investigation of nocturnal sleep was performed in nine non-ambulatory Duchenne muscular dystrophy patients (mean age 16.2 years, range 10–20) with normal daytime blood gas tensions. The data show that nocturnal sleep has some adverse influence on oxygen balance in these patients as suggested by the occurrence of arterial oxyhaemoglobin desaturation occurring mainly during REM stages. This adverse effect tended to worsen significantly within a 2-year period in the absence of any sleep-related symptoms. A significant correlation between the degree of oxygen imbalance during sleep and the degree of restrictive thoracic syndrome during wakefulness was shown.

Key words: Sleep – Respiration – Duchenne muscular dystrophy

Introduction

There is increasing interest in the study of sleep in patients with myopathies. These patients, in fact, owing to restrictive thoracic function, are at risk of developing sleep-related hypoxaemia [4], which in turn could further increase the progressive decline in respiratory and cardiac functions [2], which are already associated with the muscle disease [5]. Available information on this topic in a pure myopathy such as Duchenne muscular dystrophy (DMD) has been confined to a few, single-night, cross-sectional studies [9–10]. In particular, no data are available on the actual severity and time-course of sleep-related hypoxaemia in this disease. We report the results of a long-term clinical and polygraphic investigation of nocturnal sleep in nine non-obese, non-ambulatory DMD patients who had been previously studied cross-sectionally [7].

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Patients and Methods

The details of the patients are given in Table 1. Each patient underwent the following procedures at the time of the initial assessment and 2 years later: (1) blood chemistry, urine and haematology tests; (2) physical examination; (3) chest radiograph, echocardiogram, ECG; (4) sleep questionnaire; (5) overnight polysomnography; (6) evaluation of baseline respiratory function. Nighttime polygraphic sleep recordings were performed in the Sleep Laboratory of the Neurology Clinic, in a quiet, partially soundproof room under standard conditions of temperature and humidity. The following variables were monitored: electroencephalogram (EEG) using C3/A2, O2/A1 leads of the 10–20 international placement system; electro-oculogram (EOG: ROC/LOC); submental EMG and EMG of intercostal muscles (by surface electrodes parasternally in the second costal interspace); ECG; respiration (respiratory effort by thoracic and abdominal strain gauges; airflow by themistors placed in front of each nostril and mouth, with results integrated to give a one-signal output); snoring noise by a microphone positioned 30 cm above the patient's head; arterial oxyhaemoglobin ($HbSaO_2$) using an ear oximeter. All variables were recorded on a polygraph at a 15 mm/s paper speed. Patients retired to bed at their usual time and could remain in bed until 7.00 a.m. The light was switched off at the patient's request. None of the patients had received any sedative drug for at least 2 weeks prior to the assessment. Evaluation of baseline respiratory function during wakefulness was carried out at the Institute of Re-

Table 1. Clinical details of the patients included in the study

Patient no.	Age (years)	Chair-bound period (years)	Weight (kg)	Degree of scoliosis[a]
1	15.5	3.5	55	+++
2	21	10	52	+++
3	14	1.4	36	+
4	18.4	5.3	51	+
5	14.4	6	60	++
6	20.1	8	57	++
7	16	7.6	60	++
8	10.6	3.9	31	++
9	16.10	6.10	55	+

[a] +, mild 30°; ++, moderate 30–60°; +++, severe > 60°

spiratory Disease of the University of Pavia and consisted in blood gas determinations and spirometric measurements. The latter were performed with the patient sitting and supine, using a water-sealed Jaeger Spirometer connected to a He-analyser. To evaluate vital capacity and functional residual capacity (FRC), spirograms were recorded in a quiet and silent room for at least 10 min. Forced expiratory volume in 1 s (FEV_1) was also determined in order to rule out bronchial obstructions. Blood gas values and $HbSaO_2$ were determined with the subject in the supine position using an automatic blood gas analyser (ABL 30 Radiometer) and an ear oximeter, respectively.

Sleep recordings were scored visually according to standard criteria [8]. For the breathing patterns the following measures of respiratory pattern during sleep were considered according to international usage [1–6]: (1) apnoeas and hypopnoeas/h sleep (AHI); (2) mean $HbSaO_2$ per sleep stage; (3) magnitude of $HbSaO_2$ drop during hypopnoeas or apnoeas; (4) lowest $HbSaO_2$ value. An AHI above 5 and $HbSaO_2$ drops exceeding 5% of the mean stable value during wakefulness before falling asleep were considered pathological.

Data analysis

Spearman rank correlations were calculated in order to evaluate the relationship between the initial and the follow-up parameters. The Wilcoxon pairs rank test was used to compare parameters determined at different times. Simple linear regression analysis was used to assess the relationship between respiratory variables during sleep and some measures of respiratory function and/or of physical condition (degree of scoliosis).

Results

Clinical Data

Body weight and degree of scoliosis remained substantially stable over time.

Subjective Sleep Reports

Subjective sleep reports at the initial evaluation are summarized in Table 2. No patient reported disturbed sleep, excessive daytime sleepiness or symptoms suggestive of sleep disordered breathing. These findings did not change over time.

Objective Sleep Measures

No patient showed marked alterations of sleep patterns. All patients had a total sleep time sufficiently long to allow a correct evaluation of sleep-related breathing patterns, according to standard criteria [1]. No significant differences in sleep parameters were found between initial assessment and follow-up (Table 3).

Respiratory Variables During Sleep

At the initial assessment none of the patients met the criteria for diagnosis of sleep-apnoea (all patients showed an AHI value lower than 5). However, five out of nine patients showed $HbSaO_2$ drops greater than 5% (6–16%) of the baseline $HbSaO_2$ value recorded during wakefulness (97.7%). These desaturations occurred during infrequent, central apnoeas or hypopnoeas physiologically associated with NREM and, especially, REM sleep.

At follow-up, no patient showed an AHI value above 5. The five patients with $HbSaO_2$ drops greater than 5% at the initial assessment again showed pathological $HbSaO_2$ desaturations (6–28%). Of the remaining four patients, who had not shown any significant sleep-related modification of oxygen balance at the initial assessment, one showed $HbSaO_2$ drops greater than 5% at fol-

Table 2. Subjective nocturnal sleep reports (means ± SD) in the patients included in the study

Duration of sleep (h)	8.5 ± 1
Sleep latency (min)	14.3 ± 5
Number of mid-sleep awakenings/night	2 ± 0.8
Episodes of sleep paralysis and/or hypnagogic hallucinations	No
Snoring	Reported by 2 patients as occasional and of mild degree
Sudden awakening with gasping or difficulty in breathe	No
Morning headache, fatigue	No
Diurnal sleepiness (independent of meal times)	No

Table 3. Nocturnal sleep parameters (means ± SD) in the patients included in the study

	Initial assessment	Follow-up
TST (min)	405 ± 37	395 ± 35
SL (min)	24.3 ± 7	18.5 ± 5
SE (%)	85 ± 6.7	87 ± 5.5
NREM stage 1 (% TST)	6 ± 2	9.3 ± 4
NREM stage 2 (% TST)	43 ± 6.5	45 ± 5
NREM stage 3/4 (% TST)	25 ± 5	21.7 ± 4
Stage REM (% TST)	26 ± 3	24 ± 2
REM latency	105 ± 11	100 ± 8

TST, Total sleep time; SE, sleep efficiency; SL, sleep latency

Table 4. Respiratory parameters during nocturnal sleep (means and range): comparison between initial and follow-up recordings

	Initial assessment	Follow-up
AHI**	0.6 (0–1.3)	1.4 (0–5)
Apnoea length (s)*	20 (13–32)	22 (13–33)
Magnitude of SaO_2 drops (%)*	6 (1–16)	10 (2.5–28)
Desaturation/night**	6 (0–15)	14 (0–34)
Lowest SaO_2**	90 (83–96)	83 (68–96)
Mean $HbSaO_2$ stages 1–2 NREM	96.8 (96–97.5)	95.5 (93–97)
Mean $HbSaO_2$ stages 3/4 NREM	97.7 (96–97.5)	95.5 (93–97)
Mean $HbSaO_2$*,*** stage REM	95 (92–97)	92.2 (86–96)

* $P < 0.05$ Spearman rank order correlation
** $P < 0.025$ Spearman rank order correlation
*** $P < 0.05$ Wilcoxon pairs rank test

Table 5. Parameters of respiratory function during wakefulness in the patients included in the study (means and range)

	Initial Assessment	Follow-up
VC (lt)*·***	1.7 (1.3–2.1)	1.4 (0.6–1.9)
% of predicted value	−47.3 (−68–−21)	−58.3 (−81–−37)
FRC (lt)**	1.7 (1.3–4.0)	1.5 (1.3–3.3)
% of predicted value	−1.1 (−29–45)	11.2 (−53–31)
FEV_1 (lt)	1.4 (1.1–1.7)	1.1 (0.4–1.6)
% of predicted value	−49.3 (−66–−23)	−54.6 (−75–−35.5)
RR (c/min)***	18.9 (14.2–24.6)	19 (14.3–25.2)
$PaCO_2$ (mmHg)***	40 (37–45)	40.3 (38–44)
PaO_2 (mmHg)**	88.4 (83–94)	85 (73–96)
$HbSaO_2$ (%)**	97.5 (97–98)	96 (94–98)
Haematocrit	42 (40–44)	43 (40–46)

* $P < 0.05$ Wilcoxon pairs rank test
** $P < 0.05$ Spearman rank correlation
*** $P < 0.025$ Spearman rank correlation

VC, Vital capacity; FRC, functional residual capacity; FEV_1, forced expiratory volume in 1 s; RR, respiratory rate

low-up. Table 4 summarizes the respiratory parameters during nocturnal sleep at the initial assessment and at follow-up. Only the mean $HbSaO_2$ value during REM sleep showed a statistically significant difference between the two occasions.

Respiratory Function During Wakefulness

At the initial assessment, each patient showed a severe restrictive thoracic syndrome and marked increase of respiratory rate. No patient had evidence of bronchial obstruction. Blood gas values during wakefulness were within normal limits. After 2 years, a worsening of the restrictive thoracic syndrome was generally observed without pathological changes in blood gas values (Table 5).

Relationship Between Respiratory Function During Wakefulness and Respiratory Variables During Sleep

Both at the initial assessment and at follow-up, simple regression analysis showed a significant relationship between some parameters of oxygen desaturation during sleep (magnitude of $HbSaO_2$ drop during apnoeas and mean $HbSaO_2$ value during REM sleep) and the value of FRC during wakefulness ($P < 0.05$).

Discussion

Our longitudinal polysomnographic data confirm previous findings from cross-sectional studies, indicating that sleep-apnoea patterns are not observed in DMD patients [7–9]. Only in overweight DMD patients have sleep-apnoea patterns been found [10].

Our long-term polysomnographic study, however, shows that nocturnal sleep has some adverse influence on oxygen balance in DMD patients, as suggested by the occurrence of $HbSaO_2$ drops of a pathological degree during brief, physiologically occurring central apnoeas or hypopnoeas mainly during REM sleep. This adverse effect occurred in patients with normal $HbSaO_2$ during wakefulness and tended to worsen significantly after a 2-year period, in the absence of any subjective sleep complaint. As far as the relationship between respiratory function during wakefulness and oxygen balance during sleep was concerned, our data demonstrate a significant inverse correlation between the degree of oxygen imbalance during sleep and FRC during wakefulness. This relationship was also found in our previous cross-sectional study [7] and is in agreement with experimental data [3] indicating that low lung volumes adversely affect oxygen balance during apnoea. Our data highlight the role of the restriction syndrome per se in determining sleep-related oxygen imbalance in DMD.

In conclusion, our long-term prospective study demonstrated that nocturnal hypoxaemia occurs in DMD patients. This disorder is of a moderate degree but progresses in parallel with the worsening of the restrictive thoracic syndrome in the absence of subjective sleep complaints. Further follow-up investigations are required to evaluate the actual clinical implications of nocturnal hypoxaemia in these patients.

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