ORIGINAL ARTICLE

Respiratory function in amyotrophic lateral sclerosis patients. The role of sleep studies

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Abstract

Background and aim: Respiratory function decline in association with sleep breathing abnormalities in Amyotrophic Lateral Sclerosis (ALS) patients are fully recognized as crucial manifestations in the natural course of the disease, severely affecting the prognosis. The aim of this study was to evaluate the respiratory function at daytime and during sleep in a population of ALS patients and investigate the necessity of sleep study performance for the appropriate management of the disease.

Patients and methods: Twenty eight (10 male, 18 female) unselected patients with ALS, were evaluated in terms with their functional status by means of the ALS Functional Scale (ALSFSC**).** Baseline anthropometric measurements, pulmonary function tests and arterial blood gasses analysis were performed, as well as evaluation of patients' perception of dyspnoea. A polysomnography was performed using a multichannel ambulatory recording.

Results: Nineteen patients had sleep disordered breathing with an RDI (Respiratory Disorder Index)> 5/h (from 5.6/h to 83/h) and 10 patients had an RDI>15/h. All patients had impaired functional capacity by the ALSFSC and 11 patients (39.3%) reported mild to moderate dyspnoea. FVC was below 80% predictive value in 22 patients and in 8 patients hypoxaemia (PaO_2<80mmHg) and in 12 patients hypercapnia ($PaCO_2$>40mmHg) was present. There was no correlation found between spirometric values, maximum inspiratory and expiratory pressures and sleep study parameters. There was a significant correlation between $PaCO_2$ and RDI (r=0.498, p<0.01), and PaO_2 with nocturnal hypoxaemia (average SpO_2, r=0.436,p<0.05).

Conclusions: Sleep-breathing abnormality is common in ALS patients even in the absence of documented respiratory failure. Clinical evaluation and respiratory function tests alone may not be sufficient to predict sleep disordered breathing (SDB) and nocturnal breathing assessment should be included in the evaluation of respiratory function Hippokratia 2010; 14 (1): 33-36

Key Words: amyotrophic lateral sclerosis, sleep disordered breathing, RDI, nocturnal hypoxaemia, ALS Functional Scale (ALSFS**)**

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In ALS, the degeneration of neurons results in muscle weakness, which affects respiratory muscles in the progress of the disease. The progression of the disease is associated with a decline in respiratory function, although breathing symptoms are often mild or unrecognised by patients[1,2].

Breathing abnormality during sleep may be an early sign of respiratory dysfunction in ALS patients, but the frequency and the time of SDB occurrence are uncertain[3-5]. Yet, the relationship between pulmonary function tests and abnormal breathing during sleep is not fully understood. The aim of this study was to evaluate the respiratory function at daytime and during sleep in ALS patients and ascertain the necessity of sleep study performance for the appropriate management of the disease.

Patients and methods

Twenty eight (10 male, 18 female) unselected patients with ALS, diagnosed 1 to 48 months ago (mean duration 11.3±10.5 months) were referred to us for respiratory function evaluation. None of them had a history of chronic pulmonary disease. Their functional status was evaluated with the ALS Functional Scale (ALSFSC) that grades patients' disability. The maximum possible score is 40, with the lower score reflecting a greater level of disability[6].

Baseline anthropometric measurements (age, Body Mass Index-BMI) and pulmonary function tests were performed before sleep study. They included measurement of forced vital capacity (FVC), forced expiratory volume (FEV1) (Canshorn Medizin Electronic) maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP) (Micro Medical Respiratory Pressure Meter) and arterial blood gases while breathing room air (Radiometer Co). Patients' perception of dyspnoea was evaluated using a visual analogue scale graded from 0 (no dyspnoea at all) to 5 (severe dyspnoea).

A polysomnography was performed using the Embletta (Flaga) multichannel ambulatory recording, in a quiet room during each patients usual sleep time. This portable device measured nasal /oral flow with a pressure traducer, snoring with a microphone, thoraco-abdominal movements and oxygen saturation with a pulse oxymeter, and has accuracy equivalent to PSG[7]. Sleep apnoea and hypopnoea were defined according the standard criteria: Apnea was defined as a complete cessation of air flow lasting > 10 s; hypopnea was defined as a discernible fall in air flow lasting ≥ 10 s accompanied by a decrease in oxygen saturation of at least 3%[8].

Statistical analysis

All data are expressed as mean ± standard deviation (M±SD). Descriptive statistics were used and the Spearman's correlation coefficient test was used to explore the correlation between variables. Two sample t-test and Mann-Whitney test were used for non parametric variables between patients with normal and abnormal pulmonary tests. Statistical significance was set at $p<0.05$. Statistical analysis was performed using the SPSS v.11.5 software.

Results

All patients had impaired functional capacity in the domains examined by the ALSFSC (minimum 13, maximum 37), whereas none of the patients was obese**.** Clinical bulbar dysfunction was present in 10 patients with dysphagia and/or dysarthria and 11 patients (39.3%) reported mild to moderate dyspnoea. FVC was below 80% of predicted value in 22 patients and 25 patients had MIP $< 60cmH_2O$. In 8 patients hypoxaemia ($PaO_2 < 80mmHg$) and in 12 patients hypercapnia ($PaCO_2 > 40mmHg$) was present. There was no difference between men and women in age, in ALSFCS and in pulmonary tests, but women expressed more dyspnoea than men (2.7±1.5 and 1.5±0.9 respectively, $p<0.05$). Patients' anthropometric characteristics and respiratory function are shown in Table 1.

Nineteen patients had sleep disordered breathing with an RDI > 5/h (from 5.6/h to 83/h) and 10 patients had RDI > 15/h. The average SpO_2 before sleep onset was greater or equal to 90% in all patients. Reduction in SpO_2 during sleep was present in all patients (range of minimum SpO_2: 61% to 90%) and the index of desaturation events (ODI) ranged from 2 to 102/h. Fifteen patients spent more than 5% of recorded period with SpO_2

Table 1: Anthropometric characteristics and pulmonary function tests results in the study group.

	All patients	Men (n:10)	Women (n:18)
Age (years)	60.9±8.0	57.6±7.	63.8±8.8
ALSFSC	28.9±8	29.6±8.3	28.6±8.0
BMI kg/m²	27.7±4.2	27.2±3.1	27.9±4.7
FVC %pred	54.9±25.6	66.0±23.9	48.0±24.8
FEV1 % pred	55.9±24.1	60.3±24.7	53.0±24.1
PaO_2 mmHg	75.4±11.3	71.0±12.3	77.8±10.3
$PaCO_2$ mmHg	40.6±6.6	41.3±7.2	40.1±6.5
MIP cmH_2O	27.5±21.1	37.8±22.2	21.7±18.7
MEP cmH_2O	32.2±22.7	41.2±25.9	27.2±19.8
Dyspnea score	2.3±1.5	1.5±0.9*	2.7±1.5*

*$p<0.05$

< 90% (30.1± 29.6%) with a minSaO_2 88%. Three of the patients with RDI<5/h revealed also significant nocturnal hypoxaemia (SpO_2<90% for 26.7±18.6 % of recorded time). There were no significant differences between men and women and also between patients with and without bulbar dysfunction in respiratory events during sleep. The results of breathing function during sleep are shown in Table 2.

There was no correlation found between the duration of the disease and the FVC, the ALSFSC or any of the measured parameters during sleep. Patients with lower MIP had also lower FVC (r=0. 446, p<0.05) and higher dyspnoea score (r=-0.419, p<0.05). There was no correlation found between FVC, FEV_1, MIP, MEP and AHI, average SpO_2 and minimum SpO_2. Also there was no difference observed in measured parameters during sleep, between patients with normal (>80%prd) or reduced FVC (<80%prd).

Patients with $PaCO_2$>40mmHg had more disturbed breathing during sleep in terms of RDI(p=0.016) and longer duration of nocturnal hypoxemia (p<0.05). There was a significant correlation observed between $PaCO_2$ and RDI (r=0.498, p<0.01), and PaO_2 with nocturnal hypoxaemia (average SpO_2, r=0.436,p<0.05).

Discussion

The main finding of our study was that sleep disordered breathing is common among unselected ALS patients, and it is not correlated with daytime respiratory function tests. Furthermore, pulmonary tests and static mouth pressures were reduced in the majority of patients but this was not necessarily associated with blood gasses abnormality.

Respiratory muscle weakness, as determined by a reduction in FVC or static mouth pressures, is described in ALS patients even at the time of diagnosis and is more severe in the advanced stages of the disease[1,2,9,10]. Abnormalities in pulmonary function as a restrictive pulmonary pattern are also reported in ALS patients, but gas exchange is usually preserved at least at the early stages. This was the common pattern of pulmonary function in our patients, as 78.5% of them had reduced FVC and 89.5% reduced static mouth pressures. Gas exchange abnormalities-mainly hypercapnia- were observed in 42.8% of patients without any significant relation with pulmonary function tests,

Diaphragm dysfunction is common in ALS patients and is linked to dyspnoea and also to sleep breathing abnormalities[9,11,12]. In this study, although we used a simplified technique for diaphragmatic function assessment, the reported dyspnoea was correlated with the reduction of MIP. Women reported more severe dyspnoea than men, yet there were not significant differences between them in functional status and respiratory function. We believe that further research may be helpful to confirm and establish these sex differences,

Poor sleep with disturbed structure is reported to occur early in the course of the disease in ALS patients, with significant impact on their survival, quality of sleep and quality of life[12-14]. The most common finding is a large variety in the number of apneas and hypopneas associated with sleep hypoxemia, even in patients with preserved respiratory function during the day.

The majority of our patients had an RDI>5/h or/and severe nocturnal hypoxaemia. Hypoxaemia was mainly in association with apneas and hypopneas, but it was also present in patients without respiratory events, as it has already been reported to occur in ALS patients[15,16].

Unlike the results of others[5] the relationship between daily respiratory function and nocturnal breathing were weak in our study. The only significant correlation between blood gasses and nocturnal hypoxaemia was observed only in patients with established respiratory failure, which was rather expected. This finding reflex the fact that in patients with lower respiratory muscle strength and/or hypercapnia, sleep disordered breathing was more severe, though we did not confirm a correlation between RDI and static pressures or spirometric values. From our

Table 2: Sleep disordered breathing in ALS patients.

	All patients	Men (n:10)	Women (n:18)
Average SpO2%	92.3±2.6	92.7±1.5	92.1±3.1
RDI /h	17.4±18.8	24.1±24.6	12.9±12.7
minSpO2%	81±7.5	80.5±8.2	81.0±6.9
ODI	20.4±2.0	30.2±29.1	15.0±15.3
t <90%	16.5±29.0	12.2±13.8	19.3±30.7

results we speculate that the performance of daily pulmonary function tests alone is not enough to detect respiratory dysfunction during sleep in ALS patients. These results are in agreement with others, who suggested that sleep study in ALS patients is a valuable screening test for the early diagnosis of SDB and moreover for the early use of non invasive ventilation[16].

A possible limitation of our study was the absence of an EEG to confirm sleep structure disturbances and also to examine in detail the observed hypoxaemia, which was not associated with apneas/hypopneas. The portable device we used has as a high accuracy as standard polysomnography[7] and also gives more information of sleep breathing than simple overnight oximerty. We suggest that the use of portable devices in daily routine facilitate the early detection of SDB, which is essential for the appropriate management of respiratory dysfunction in these patients.

In conclusion, sleep-breathing abnormality is common in ALS patients in the absence of documented respiratory failure. In our study the daytime function in ALS patients did not reflect the breathing during sleep, supporting the view that clinical evaluation and respiratory function tests alone may not be sufficient to predict SDB and nocturnal breathing assessment should also be performed

Conflict of interest: none.

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