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Original Article

Sleep apnea and periodic leg movements in the first year after spinal cord injury ☆

Paola Proserpio [a], Andrea Lanza [a], Katrina Sambusida [a], Lara Fratticci [b], Pamela Frigerio [c], Maurizio Sommariva [d], Enrica Giuliana Stagni [c], Tiziana Redaelli [c], Fabrizio De Carli [e], Lino Nobili [a,e,*]

[a] *Centre of Sleep Medicine, Centre for Epilepsy Surgery "C. Munari", Niguarda Hospital, Milan, Italy*
[b] *Institute of Neurology, "Humanitas" Clinical Institute, Milan, Italy*
[c] *Spinal Cord Unit, Niguarda Hospital, Milan, Italy*
[d] *Emergency Department, Niguarda Hospital, Milan, Italy*
[e] *Institute of Bioimaging and Molecular Physiology, Genoa Unit, National Research Council, Genoa, Italy*

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ABSTRACT

Background: Sleep disturbances are frequently reported by patients with spinal cord injury (SCI). Studies have shown an increased incidence of sleep-disordered breathing (SDB) and periodic leg movements during sleep (PLMS) in people with stable long-term SCI.
Methods: This was a prospective observational study in order to evaluate the features and possible predisposing factors of SDB and PLMS in a heterogenic population of consecutive SCI patients admitted at the Spinal Unit of the Niguarda Hospital within the first year after injury. Each patient underwent a clinical assessment, full polysomnography, and arterial blood gas analysis before and immediately after sleep. Multiple logistic regressions were applied in order to evaluate factors associated with SDB and PLMS.
Results: Thirty-five (15 tetraplegic and 20 paraplegic) patients were enrolled. Nine patients (25.7%) had an obstructive SDB and 10 (28.6%) had PLMS. The frequency of SDB was higher in tetraplegic with respect to paraplegic patients (Wald statistic: 7.71; $P = 0.0055$), whereas PLMs were significantly more frequent in patients with an incomplete motor lesion than in subjects with a complete motor lesion (Wald statistic: 6.14; $P = 0.013$).
Conclusion: This study confirms a high frequency of SDB and PLMS in SCI patients in the first year following injury. Independently from possible sub-acute and chronic clinical variables, the level and the completeness of the spinal cord lesion are the main factors associated respectively with an early development of SDB and PLMS.

1. Introduction

Dysfunctional sleep is frequently reported in patients with spinal cord injury (SCI) [1,2]. This is partly related to neurogenic pain, spasticity, and other medical conditions resulting from the spinal cord lesions and also to specific sleep-related disorders, such as sleep-disordered breathing (SDB) or periodic leg movements during sleep (PLMS) [3,4].

Different studies have shown an increased incidence of SDB in people with SCI [3,5–11]. Indeed, despite differences in methodology and patient selection (low representation of women and paraplegic patients), the medical literature indicates a prevalence of SDB in patients with SCI that is at least twice the reported prevalence in the general population [7,8,10]. Moreover, among SCI patients, subjects with cervical lesions seem to be more prone to develop SDB [12]; and, within SDB, obstructive sleep apnea rather than central sleep apnea predominates [8,13]. However, the pathogenic mechanisms that cause SDB in SCI patients are still unclear. In particular, there are no data about the onset time of SDB because the majority of these studies have been conducted several years after injury [5–8,10], whereas only two recent studies investigated the SDB during the acute phase of SCI [9,11].

Moreover, limited data are available on the presence of PLMS in SCI. Indeed, available studies consist only of small case series that included stable long-term SCI patients [14–17].

The aim of our study was to evaluate the features and possible factors associated with SDB and PLMS in a heterogenic population of SCI patients (paraplegic and tetraplegic patients with complete or incomplete lesions) during the first year after injury.

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* Corresponding author. Centre of Epilepsy Surgery "C. Munari", Center of Sleep Medicine, Niguarda Hospital, Piazza Ospedale Maggiore 2, 20162 Milan, Italy. Tel.: +39 0264447323; fax: +39 0264442874.
E-mail address: Lino.nobili@ospedaleniguarda.it (L. Nobili).

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2. Methods

2.1. Study design

This was a prospective observational study. A consecutive series of patients admitted at the Spinal Unit of the Niguarda Hospital, Milan, Italy, was analyzed during the first year after SCI from September 2010 to December 2011. Exclusion criteria were inability to give informed consent, significant head injury (amnesia >24 h post injury, evidence of cerebral contusion on computed tomography), presence of tracheostomy at time of enrollment, ventilator dependent at time of enrollment, and other respiratory problems (chest infection, pneumothorax, hemothorax, effusion, intercostal catheter).

Each patient underwent a clinical assessment and full polysomnography.

Clinical assessments included body mass index (BMI, body weight/height squared, kg/m^2), neck circumference, oral anatomy according to Mallampati et al. [18] and medication usage.

The location of the lesion and its extent were assessed in each patient by magnetic resonance imaging, evoked potential, and electromyography. Motor and sensory examinations were performed and all patients were classified using the American Spinal Injury Association (ASIA) impairment scale A–D [19]. A visual analogic scale (VAS) was used to assess the degree of daytime sleepiness. The Berlin Questionnaire [20] was used in order to evaluate possible presence of SBD preceding the injury (written permission had been obtained for its use).

A standard overnight full polysomnography was performed on the ward in an attended setting (AURA®; PSG Ambulatory Systems GRASS Technologies, Warwick, RI, USA). In accordance with standard criteria [21], the recording included: electroencephalography (at least three channels), bilateral electro-oculography, chin and tibial electromyography, electrocardiography, oronasal airflow, chest and abdominal effort (recorded using respiratory inductance plethysmography), pulse oximetry, and sensor of body position. All studies were manually reviewed by a medical doctor expert in sleep medicine, certified by the Italian Association of Sleep Medicine. Sleep was staged and respiratory and motor events were scored according to standard criteria [21].

The SDB was classified as mild if the apnea–hypopnea index (AHI, number of respiratory events per hour of sleep) was between 5 and 15, moderate if the AHI was between 15 and 30, and severe if the AHI was >30. All patients underwent arterial blood gas analysis before and immediately after sleep in order to assess the presence of hypoventilation during sleep [21].

The periodic leg movements index (PLMI) was defined as the number of PLM per hour of sleep.

LM was not scored if it occurred during a period from 0.5 s preceding an apnea or hypopnea to 0.5 s following an apnea or hypopnea [21]. Consistent with the ICSD-2 criteria [22], PLMI >15 was used as the cut-off criterion for the presence of PLMS.

All patients gave written informed consent before enrollment. The study was approved by the ethics committee of the Niguarda Hospital (Milan, Italy; record no. 991).

2.2. Statistical analysis

For descriptive statistics, clinical and polysomnographic data were summarized for tetraplegic and paraplegic patients (Tables 1 and 2), for patients with and without SDB (Table 3), and patients with and without PLMS (Table 4). A comparison between the two groups was independently performed for each variable by applying an appropriate test: the parametric *t*-test for interval variables with approximately normal distribution (after log or logit transformation when required), the Mann–Whitney *U*-test for interval variables with clearly non-normal distribution, and the Fisher exact test for dichotomic variables.

In order to evaluate factors associated with SDB, the multiple logistic regression with SDB classification (absent/mild/moderate/severe) was applied as ordinal dependent variable, with the following as independent variables (five categorical and four interval variables): gender (M/F), lesion site (cervical/other), lesion completeness (complete/incomplete), Mallampati score >2, muscle relaxant drugs use, age, BMI, neck circumference, and time elapsed since injury event. Forward stepwise selection was applied in order to identify significant factors.

The same multiple logistic regression method was applied to identify factors associated with presence of PLMS (PLMI >15). In this case, five categorical variables (gender, lesion site, lesion completeness, use of antidepressant, and use of antiepileptic drugs) and two interval variables (age and time since the injury event) were considered and selected by forward stepwise analysis.

Statistical analyses were performed with the Statistica version 10 software package (StatSoft, Inc., Tulsa, OK, USA).

Table 1
Demographic features of the studied population.

	Total (*n* = 35)	Tetraplegic (*n* = 15)	Paraplegic (*n* = 20)
Age (years)[a]	38.2 (16.3)	43.7 (18.7)	34.1 (13.3)
Male/female	29/6	13/2	16/4
BMI (kg/m^2)[a]	23 (2.8)	23.6 (2.3)	22.6 (3.1)
Neck circumference (cm)[a]	36.7 (3.3)	37.9 (3.1)	35.9 (3.4)
Completeness of SCI (ASIA scale)			
A	17	4	13
B	4	2	2
C	12	8	4
D	2	1	1
Time since injury (days)[a]	77 (68)	78.7 (74.6)	69.8 (57.8)
Daytime sleepiness (VAS ≥5)	5	2	3
Drugs			
Benzodiazepines	24	9	15
Opioids	14	8	6
Serotoninergic antidepressants	17	7	10
Tricyclic antidepressants	4	2	2
Muscle relaxants	12	7	5

Abbreviations: BMI, body mass index; SCI, spinal cord injury; ASIA, American Spinal Injury Association; VAS, visual analogic scale.
[a] Mean (standard deviation).
General clinical features were not significantly different in tetraplegic patients with respect to paraplegic ones.

Table 2
Polysomnographic parameters of the studied population.

	Total (*n* = 35)	Tetraplegic (*n* = 15)	Paraplegic (*n* = 20)
TST (min)[a]	458.4 (91.9)	450.8 (91.5)	464 (94.2)
N1 (% of TST)[a]	13.7 (9.1)	15.8 (10.1)	12.1 (8.2)
N2 (% of TST)[a]	49.1 (12.1)	49.7 (12.6)	47.5 (12.8)
N3 (% of TST)[a]	21.8 (11.7)	19.4 (14.7)	23.6 (8.8)
REM (% of TST)[a]	15.5 (7.8)	15.1 (8.1)	15.7 (7.9)
AHI[a]	6.7 (14)	13.9 (19.4)	1.4 (1.7)*
ODI[a]	8.2 (16.2)	16 (22.4)	2.4 (4)**
AHI >5	9	8	1***
PLM index[a]	25.6 (44.4)	31.4 (46.4)	23.8 (62)
PLMS (PLM index >15)	10	6	4

Abbreviations: TST, total sleep time; N1, sleep stage N1; N2, sleep stage N2; N3, sleep stage N3; REM, rapid eye movement sleep; AHI, apnea–hypopnea index; ODI, oxygen desaturation index; PLMS, periodic leg movements in sleep.
[a] Mean (standard deviation).
AHI and ODI were significantly higher in tetraplegic patients: *Mann-Whitney *U*-test, $P = 0.013$; **Mann-Whitney *U*-test, $P = 0.016$; ***Fisher's exact test, $P = 0.0019$.