Journal of Sleep Disorders & Therapy
ISSN: 2167-0277

Sacchetti et al., J Sleep Disorders Ther 2013, 2:2
DOI: 10.4172/2167-0277.1000113

Research Article Open Access

Sleep Disordered Breathing after Stroke: Clinical Profile of Patients with Obstructive- as Opposed to Central-Sleep Apnea

Maria Luisa Sacchetti[1]*, Maria Teresa Di Mascio[1], Giacomo Della Marca[2], Antonio Minni[3], Silvia Ottaviani[1], Danilo Toni[1] and Marco Fiorelli[1]

[1]*Department of Neurology and Psychiatry, Sapienza University, Rome, Italy*
[2]*Sleep Unit, Institute of Neurology, Catholic University, A. Gemelli, Rome, Italy*
[3]*Department of Sensory Organs, Sapienza University of Rome, Rome, Italy*

Abstract

Aim: In order to define the clinical and instrumental profile of patients with Obstructive Sleep Apnea/Hypopnea (OSAH) and to compare them with that of cases with Central Sleep Apnea/Hypopnea (CSAH), a series of stable strokes were studied.

Methods: Thirty four patients were submitted to both clinical and polisomnographyc study (PSG) after 4 months of stroke. A Sleep Disordered Breathing (SDB) was diagnosed in all cases with an AHI>5. Patients were classified as affected by predominantly OSAH (*p*OSAH), predominantly CSAH (*p*CSAH), or normal patients. Comparisons were made among the groups and correlation analyses were done in each group. Significance was set at p<0.005.

Results: Thirty-four ischemic strokes were enrolled (55% embolic, 6% large artery, 32% lacunar, 9% with undetermined cause). The 76% of them had a SDB (pOSAH=61%; pCSAH=39%). Nearly the 47% of cases had an obstruction of the upper airways alone or combined with an increase in pharyngeal tissue. No significant differences were found between *p*OSAH and *p*CSAH. In *p*OSAH cases, 8 cases (50%) had an obstruction of the upper airways; in 4 of them it was combined with an increase in pharyngeal tissue; the time interval from stroke to PSG (Δ t), was inversely related to both TST (p 0.017) and TSP (p 0.039); the NIH-SS at entry was directly related to the number of arousals /h of sleep (p 0.044); the more severe AHI the higher is ODI (p 0.000). In the pCSAH group, 4 cases (40%) had an obstruction of the upper airways combined with an increase in pharyngeal tissue; two of these 4 cases had also a BMI>30. In CSAH, Δt was inversely related to SE Index (p 0.021), and directly related to both the number of arrhythmias/h sleep (p 0.016) and ODI (p 0.033). No correlations were found between the number of arrhythmias/h sleep and causes of stroke both in *p*OSAH and in *p*CSAH groups.

Conclusions: Our data suggest a direct effect of stroke on the peripheral breathing system with subsequent alteration of loop gain and CSAH phenotype, at least in a subgroup of cases. To confirm this hypothesis multicenter clinical sleep studied are needed.

Keywords: Sleep apnea; Stroke; Loop gain; Cycling alternating patterns

Introduction

Prevalence of Sleep-Disordered Breathing (SDB) in patients with first-ever stroke or TIA is higher than in normal populations [1]. The disturb more frequently recognized in these cases is a 'mixed' rather than purely obstructive or central disorder [1,2]. In some cases, what starts as clearly obstructive disease, evolves into predominantly central by the end of the recording [3,4]. This phenomenon has been reported to frequently occur in patients affected by Congestive Heart Failure (CHF) [4,5]; more often it is precipitated by the Continuous Positive Airway Pressure (CPAP) treatment of an obstructive sleep apnea/hypopnea (OSAH) [6-8]. Characteristics of SDB in patients with stable stroke have not been studied jet.

In order to define the clinical and instrumental profile of patients affected by OSAH and to compare them with the profile of cases affected by a Central Sleep Apnea/Hypopnea (CSAH), we report here data on a series of 34 cases with stable stroke, studied at Sapienza, University of Rome.

Methods

Patients

A consecutive series of patients with acute stroke, admitted to the Stroke Unit of Policlinico Umberto I University Hospital, were screened. After the exclusion of patients who did not consent to enter the study, elected cases were submitted to both clinical and instrumental diagnostic tests at 4 months of stroke onset. Stroke risk profile was assessed, and then classified, according to the Italian SPREAD guidelines [9]. Participants were visited firstly at stroke onset and at discharge from the Stroke Unit, and then on the day of the polisomnographic Study (PSG). The severity of neurological deficit was assessed by means of NIH-SS [10,11]. Causes of stroke were classified as to TOAST criteria [12]. Daytime sleepiness was estimated with the Epworth Sleepiness Scale questionnaire (ESS) [13]. The presences of symptoms other than daytime sleepiness have also been investigated, and classified so as: choking, gasping, fragmented sleep, unrefreshing sleeps, reported daytime sleepiness, inattention, accordingly with guidelines [13,14]. In order to identify conditions predisposing to OSAHS, an otorhinolaryngology's (ORL) evaluation was performed.

***Corresponding author:** Maria Luisa Sacchetti, Department of Neurology and Psychiatry, Sapienza University, Rome, Italy, Tel: +39 06 4453610; E-mail: marialuisa.sacchetti@uniroma1.it

Received April 01, 2013; **Accepted** April 20, 2013; **Published** April 25, 2013

Citation: Sacchetti ML, Di Mascio MT, Marca GD, Minni A, Ottaviani S, et al. (2013) Sleep Disordered Breathing after Stroke: Clinical Profile of Patients with Obstructive- as Opposed to Central-Sleep Apnea. J Sleep Disorders Ther 2: 113. doi:10.4172/2167-0277.1000113

Sleep studies and polysomography

The ambulatory PSG study was performed by the hand-held 34 channel Morpheus Ambulatory recorder by Micromed® S.r.l. Ambulatory 34 Channels PSG was preferred to standard laboratory recording in order to allow the patients to sleep in their home setting, without needs of adaptation. The following parameters were recorded: 1) body position; 2) rib-gage and abdominal respiratory efforts (Dual thoracoabdominal RIP -respiratory inductance Plethysmography-belts by Micromed® S.r.l. Accessories EPM 915x A); oro-nasal airflow (thermistor transducer by Micromed® S.r.l. Accessories EPMs 1450-S); 4) haemoglobin saturation (finger pulse oximeter sensor); 5) 8 EEG channels (2 frontal, 2 central, 2 temporal, 2 occipital); 6) right and left electrooculography, and 7) sub mental electromyography from surface electrodes; 8) Electrocardiogram (EKG). Morpheus was retrieved the following morning the sensors were attached; data were downloaded to the SystemPlus Evolution software, and subsequently analyzed with dedicated software Rembrandt Sleep View, by a sleep expert. Were considered adequate only PSGs with a total recording time >4 hours and a Total Sleep Time (TST) >2 hours, with presence of both NREM and REM sleep episodes. Sleep-stage scoring was done visually according to standard criteria [15].

Definitions

Apnea was defined as the cessation of airflow for at least 10 seconds. Hypopnea was defined a reduction less than a 50% from baseline of a valid measure of breathing during sleep, associated with an arousal or with an oxygen desaturation of >3%. Apnoea-Hypopnoea Index (AHI) was the sum of all apneas and hypopneas occurring per hour of sleep. Sleep Disordered Breathing (SDB), either central or obstructive, was diagnosed in presence of an Apnea/Hypopnea Index (AHI) value>5 [13]. Three different degrees of severity were outlined: Mild SDB: AHI value > 5 ≤ 15; Moderate SDB: AHI value >15 ≤ 30; Severe SB: AHI value >30 [16]. Each event without associated chest wall movement was considered as central in origin (CSAH). A diagnosis of OSAHS was set in cases in whom at least 50% of the total respiratory events showed a clear dissociation between preserved chest wall movement and airflow pattern with a decrease in the amplitude >50% from baseline, and lasting at least 10 seconds (*p*OSAH). A CSAHS was instead diagnosed when at least 50% of the total respiratory events were central in origin (*p*CSAH). Central Periodic Breathing (CPB) was defined so as recommended [17]. Arousals were defined as "an abrupt change from a "deeper" stage of non-REM (NREM) sleep to a "lighter" stage, or from REM sleep toward wakefulness, with the possibility of awakening as the final outcome" [18]. Arrhythmias were defined as any disturbances of the normal rhythmic beating of the heart.

Statistical analysis

On the bases of PSG study, 3 groups were identified: patients with normal sleep study, cases with predominantly OSAHS (*p*OSAH), and cases with predominantly CSAHS (*p*CSAH). Groups were compared in terms of: age, sex, time from stroke to PSG evaluation (days); NIH-SS at entry and at discharge from Stroke Unit; Body Mass Index (BMI), ESS, TST; Total Sleep Period (TSP); Sleep Efficiency Index; arousal /h sleep; sleep phases; number and type of apneas and hypopneas; arrhythmias of sleep; total number of central apneas-hypopneas per hour of sleep; total number of obstructive apneas-hypopneas per hour of sleep; and Oxygen Desaturation Index (ODI). Patient's demographic data, risk factors for stroke, and sleep study data are expressed as mean and SD or percentages. Statistical comparisons between groups were made using ANOVA, χ^2 or Fisher exact test, depending on which was more appropriate. Correlation analyses were done with non-parametric tests (Spearman's rho). Statistical significance was set at $p<0.05$. Statistical analysis was performed with Statistical Package of Social Sciences (SPSS) version 18.0 for Windows.

Results

After the exclusion of patients who did not consent, 34 cases entered the study. All had an ischemic stroke. The 55% (n=18) were embolic in nature, the 32% (n=11) were lacunar, in the 9 % (n=3) of cases the cause of stroke was undetermined, and in 6% (n=2) a large artery cause was revealed. Patients' mean age was 62.4 ± 14.6. Sixteen cases had a mild (AHI value>5 ≤ 15), 8 had a moderate (AHI value>15 ≤ 30) and 2 cases a severe SDB (AHI value > 30). Sixteen out of the 26 cases with an AHI ≥ 5 (61.5%) had a predominantly OSAH (*p*OSAH), and 10 cases (38.5%) had a predominantly CSAH (*p*CSAH). None of the patients affected by *p*CSAH presented central periodic breathings during sleep (CPBS). The BMI was 28 ± 6 kg/m^2 (range 21 to 47; median 26.5). The mean AHI was 12 ± 9 (range 1 to 35; median 10.5). The PSG study was performed 126.4 ± 49 days after stroke onset (range: 66-282; median 113,5 days). The ORL evaluation was performed in 32 cases and was abnormal in 15 of them. Fourteen cases had an obstruction of the upper airways and in 8 of them the obstruction was combined with an increase in pharyngeal tissue. Eight patients with positive ORL evaluation had a *p*OSAH at the PSG and 4 were affected by *p*CSAHS. All these 4 cases who presented at PSG a *p*CSAH had an obstruction of the upper airways combined with an increase in pharyngeal tissue; two of them had a BMI>30.

The profile of cases respectively affected by *p*OSAH and *p*CSAH are reported in table 1.

No significant difference was found between *p*OSAH and *p*CSAH cases (Table 1). In the group of cases with *p*OSAH the PSG study was performed 147.1 ± 63,2 days after stroke onset (range: 92-282; median 124,5 days). Correlation analysis highlighted that the time interval from stroke to PSG (Δ t) was inversely correlated with both TST (p=0.017) and TSP (p 0.039); the NIH-SS score at entry significantly correlated to the number of arousals /h of sleep (p=0.044); finally, the more severe AHI the higher is ODI (p=0.000). In the group of cases with *p*CSAH the PSG study was performed 113.5 ± 18,5 days after stroke onset (range: 87-140; median 110,5 days). In this group the only significant correlations found were between Δ t and SE Index (inverse correlation; p 0.021) and between Δ t and both arrhythmias/h sleep (p=0.016) and ODI (direct correlation; p=0.033). No significant correlation was found between the number of arrhythmias/h sleep and causes of stroke as to the TOAST criteria (p=0.164) either in the group of cases with *p*OSAH and *p*CSAH.

Discussion

In our series of cases, nearly the 76% of patients had an abnormal breathing during sleep; the 61% of them were predominantly obstructive, and the 39% were predominantly central events.

Patients with predominantly CSAH did not differ significantly to OSAH in demographic characteristics, stroke risk profile, and sleep study parameters. Paradoxically, some of cases with predominantly CSAH are affected also by conditions that would better explain a severe OSAH. In fact, 4 out of 10 cases with *p*CSAH had an obstruction of the upper airways combined with an increase in pharyngeal tissue; in two of them also a BMI higher than 30 was documented. This result may indicate that the predominance of CSAH over OSAH is just phenotypical and that in certain cases, stroke itself is responsible

		Controls	*p*OSAH	*p*CSAH	p values
		n=8	n=16	n= 10	
Demographics	Age mean ± SD	55.1 ± 19	60.2 ± 12.4	72 ± 11*	0.032
	Males n (%)	6 (75)	8 (50)	8 (80)	0.233
Clinical	NIH-SS at entry mean ± SD	3 ± 3	5.1 ± 3.6	3.6 ± 2.5	0.780
characteristics	NIH-SS at discharge mean ± SD	1.5 ± 1.4	2.2 ± 1.9	1.3 ± 1.8	0.740
	BMI mean ± SD	28.5 ± 7.8	27.41 ± 5.3	28.4 ± 4	0.976
	AHI mean ± SD	2.3 ± 0.9	15.3 ± 8.7*	15.3 ± 8.2*	0.001
	BMI ≥ 30 n (%)	2 (5.9)	3 (8.8)	4 (11.8)	0.480
	ESS mean ± SD	1.9 ± 2.5	7.7 ± 4.6*	6.8 ± 4.9	0.013
	Obstruction of the upper airways n (%)	2 (6.7)	8 (26.7)	4 (13.3)	0.050
	Increase in pharyngeal tissue n (%)	0 (0)	4 (11.8)	4 (11.8)	0.333
Risk factors	Hypertension n (%)	5 (62.5)	11 (68.8)	8 (80.0)	0.703
for stroke	Smoke n (%)	4 (50.0)	5 (31.1)	5 (50)	0.540
	Atrial fibrillation n (%)	1 (12.5)	5 (31.3)	5 (50)	0.237
	ICA stenosis n (%)	2 (25.0)	7 (43.8)	2 (20)	0.397
	Diabetes n (%)	0 (0)	5 (31.3)	2 (20)	0.203
	Previous TIA n (%)	0 (0)	3 (18.8)	2 (20)	0.404
	Ischemic heart disease n (%)	0 (0)	5 (31.3)	3 (30)	0.199
	Patent foramen ovale n (%)	3 (37.5)	4 ((25)	1 (10)	0.385
	Hyperomocisteinemia n (%)	0 (0)	2 (12.5)	1(10)	0.558
	Hypercholesterolemia n (%)	6 (75)	12 (75)	6 (60)	0.682
	Congestive heart failure n (%)	0 (0)	2 (12.5)	0 (0)	0.302
PSG data	Days between stroke and PSG (Δ t) mean ± SD	100.9 ± 18.7	147.1 ± 63.2	113.5 ± 18.5	0.701
	Total Sleep Time (in minutes) mean ± SD	414.4 ± 85.9	344.4 ± 134.3	333 ± 122	0.182
	Total Sleep Period (in minutes) mean ± SD	488 ± 87.9	427.7 ± 137.1	496.5 ± 96.4	0.783
	Sleep Efficiency Index mean ± SD	81.3 ± 13	74.3 ± 19	63.6 ± 26.5	0.073
	Arousals/h sleep (in thousands) mean ± SD	32 ± 16	39 ± 18	42.5 ± 14.8	0.205
	Arrhythmias /h sleep mean ± SD	15.3 ± 37	73.8 ± 167.8	238 ± 272.9*	0.020
	ODI mean ± SD	7.4 ± 14	15.6 ± 11	13.9 ± 6.5	0.240
	Symptoms other than Daily Sleepiness n (%)	1 (12.5)	10 (62.5)	7 (70)*	0.030
	OSAHS before stroke n (%)	0 (0)	1 (6.3)	1 (10)	0.666

Fisher exact Test, or Anova as appropriate. Significance is set at 0.05
*=significant difference with controls

Table 1: Patients demographic data, clinical characteristics, risk factors for stroke, PSG data, and comparisons respectively between OSAHs, CSAHs, and controls.

for the new onset of an OSAH (or of the worsening of a pre-existing one); in a group of those cases, cause of complex, and only partially understood pathophysiological mechanism (loop gain >1, altered chemo sensitivity), the central drive to breathe may be altered so as to result in the absence of efforts to breath, i.e. central sleep apnea [19,20]. In *p*OSAH cases, the NIH-SS score at entry significantly correlated to the number of arousals of sleep. Given that one of the most significant indicators of sleep efficiency is the number of arousals per hour of sleep, it seems as if the more severe the neurological deficit at the onset of stroke, the less efficient the breathing at the long term. One possible explanation of this phenomenon is that stroke affects airways anatomy or function proportionally to the severity of neurological deficit. The tendency toward a significant correlation between stroke severity at entry and the total number of OSAH events (p 0.080), allows not deny this hypothesis. In the group of cases with *p*OSAH, the more severe AHI the higher is ODI; not the same in *p*CSAH. Actually cases affected by central apnea are able to maintain the O2 saturation within normal values more easily than *p*OSAHs. Nonetheless, this datum conflicts with interpreting *p*CSAHs as more severe *p*OSAHs with altered loop gain, and goes instead in the direction of a role of stroke on patients' CAP (Cycling Alternating Patterns). In this case, the lack of differences between *p*OSAH and *p*CSAH events may consist in the fact that stroke causes the fragmentation of sleep and of altered CAP; in order to elucidate differences in *p*OSAH and *p*CSAH CAP's, more insights into the relationship between the microstructure of sleep and the sleep disordered breathing after stroke are required [21].

Correlation analysis highlighted that the longer the time interval from stroke to PSG the higher AHI and ODI, the shorter both the TST and TSP, the lower the Sleep Efficiency index, as if time has a negative influence both on the quality of sleep and on its duration. Also this result goes in the direction of SDB as a consequence of stroke on the microstructure of sleep [22]. Given the influence of depression on CAP, of great interest would be to elucidate its role on stroke patients' CAP, either affected by *p*OSAH or *p*CSAH.

Sleep studies on stroke populations demonstrate they are affected by some mix of OSAH and CSAH, as if these disturbances are the result of an interaction between the patients' primary breathing condition and some of the long term consequences of stroke on the breathing system (altered loop gain), or on the microstructure of sleep (i.e. CAP system) [1,2,23-25].

The presence of patients affected by obstruction of the upper airways combined with an increase in pharyngeal tissue and a higher than 30 BMI, among cases with predominantly central sleep apnea, goes in the direction of an altered loop gain, probably in cases with

severe OSA. This might explain the higher rates of predominantly central sleep apnoea-hypopneas of our series.

Many questions about the SDB profile after stroke are unanswered. Multicenter clinical sleep studied, properly designed to answer these questions are needed.

Acknowledgement

Funded by Sapienza, University of Rome on year 2010. Grant n. C26A10E3ST.

References

1. Johnson KG, Johnson DC (2010) Frequency of sleep apnea in stroke and TIA patients: a meta-analysis. J Clin Sleep Med 6: 131-137.
2. Bassetti C, Aldrich MS (1999) Sleep apnea in acute cerebrovascular diseases: final report on 128 patients. Sleep 22: 217-223.
3. De Paolis F, Colizzi E, Milioli G, Grassi A, Riccardi S, et al. (2013) Complex sleep apnea syndrome in stroke patients. Sleep Med 14: 224.
4. Tkacova R, Niroumand M, Lorenzi-Filho G, Bradley TD (2001) Overnight shift from obstructive to central apneas in patients with heart failure: role of PCO2 and circulatory delay. Circulation 103: 238-243.
5. Ryan CM, Bradley TD (2005) Periodicity of obstructive sleep apnea in patients with and without heart failure. Chest 127: 536-542.
6. Morgenthaler TI, Kagramanov V, Hanak V, Decker PA (2006) Complex sleep apnea syndrome: is it a unique clinical syndrome? Sleep 29: 1203-1209.
7. Gilmartin GS, Daly RW, Thomas RJ (2005) Recognition and management of complex sleep-disordered breathing. Curr Opin Pulm Med 11: 485-493.
8. KuÅºniar TJ, KovaÄ eviÄ‡-RistanoviÄ‡ R, Freedom T (2011) Complex sleep apnea unmasked by the use of a mandibular advancement device. Sleep Breath 15: 249-252.
9. Gensini GF, Dilaghi B, Zaninelli A (2006) Italian SPREAD Guidelines: from past to future. Neurol Sci 27 Suppl 3: S254-257.
10. Pezzella FR, Picconi O, De Luca A, Lyden PD, Fiorelli M (2009) Development of the Italian version of the National Institutes of Health Stroke Scale: It-NIHSS. Stroke 40: 2557-2559.
11. Muir KW, Weir CJ, Murray GD, Povey C, Lees KR (1996) Comparison of neurological scales and scoring systems for acute stroke prognosis. Stroke 27: 1817-1820.
12. Madden KP, Karanjia PN, Adams HP Jr, Clarke WR (1995) Accuracy of initial stroke subtype diagnosis in the TOAST study. Trial of ORG 10172 in Acute Stroke Treatment. Neurology 45: 1975-1979.
13. Johns MW (1991) A new method for measuring daytime sleepiness: the Epworth sleepiness scale. Sleep 14:540-545.
14. Thorpy MJ. American Academy of Sleep Medicine.ICSD-2(2005)-International Classification of Sleep Disorders, 2nd edition:Diagnostic and coding Manual American Academy of Sleep Medicine. 2005.
15. Kushida CA, Littner MR, Morgenthaler T, Alessi CA, Bailey D, et al. (2005) Practice parameters for the indications for polysomnography and related procedures: an update for 2005. Sleep 28: 499-521.
16. Epstein LJ, Kristo D, Strollo PJ Jr, Friedman N, Malhotra A, et al. (2009) Clinical guideline for the evaluation, management and long-term care of obstructive sleep apnea in adults. J Clin Sleep Med 5: 263-276.
17. Berry RB, Budhiraja R, Gottlieb DJ, Gozal D, Iber C, et al. (2012) Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. J Clin Sleep Med 8: 597-619.
18. (1992) EEG arousals: scoring rules and examples: a preliminary report from the Sleep Disorders Atlas Task Force of the American Sleep Disorders Association. Sleep 15: 173-184.
19. Younes M, Ostrowski M, Thompson W, Leslie C, Shewchuk W (2001) Chemical control stability in patients with obstructive sleep apnea. Am J Respir Crit Care Med 163: 1181-1190.
20. Younes M (2008) Role of respiratory control mechanisms in the pathogenesis of obstructive sleep disorders. J Appl Physiol 105: 1389-1405.
21. Thomas RJ, Terzano MG, Parrino L, Weiss JW (2004) Obstructive sleep-disordered breathing with a dominant cyclic alternating pattern-a recognizable polysomnographic variant with practical clinical implications. Sleep 27: 229-234.
22. Parrino L, Ferri R, Bruni O, Terzano MG (2012) Cyclic alternating pattern (CAP): the marker of sleep instability. Sleep Med Rev 16: 27-45.
23. Parra O, Arboix A, Bechich S, García-Eroles L, Montserrat JM, et al. (2000) Time course of sleep-related breathing disorders in first-ever stroke or transient ischemic attack. Am J Respir Crit Care Med 161: 375-380.
24. Dziewas R, Humpert M, Hopmann B, Kloska SP, Lüdemann P, et al. (2005) Increased prevalence of sleep apnea in patients with recurring ischemic stroke compared with first stroke victims. J Neurol 252: 1394-1398.
25. Bassetti CL (2005) Sleep and stroke. Semin Neurol 25: 19-32.