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Original Article

Sleep-disordered breathing among acute ischemic stroke patients in Brazil

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ABSTRACT

Objectives: Sleep-disordered breathing (SDB) is very common in acute stroke patients and has been related to poor outcome. However, there is a lack of data about the association between SDB and stroke in developing countries. The study aims to characterize the frequency and severity of SDB in Brazilian patients during the acute phase of ischemic stroke; to identify clinical and laboratorial data related to SDB in those patients; and to assess the relationship between sleep apnea and functional outcome after six months of stroke.

Methods: Clinical data and laboratorial tests were collected at hospital admission. The polysomnography was performed on the first night after stroke symptoms onset. Functional outcome was assessed by the modified Rankin Scale (mRS).

Results: We prospectively evaluated 69 patients with their first-ever acute ischemic stroke. The mean apnea–hypopnea index (AHI) was 37.7 ± 30.2. Fifty-three patients (76.8%) exhibited an AHI ≥ 10 with predominantly obstructive respiratory events (90.6%), and thirty-three (47.8%) had severe sleep apnea. Age (OR: 1.09; 95% CI: 1.03–1.15; $p = 0.004$) and hematocrit (OR: 1.18; 95% CI: 1.03–1.34; $p = 0.01$) were independent predictors of sleep apnea. Age (OR: 1.13; 95% CI: 1.03–1.24; $p = 0.01$), body mass index (OR: 1.54; 95% CI: 1.54–2.18; $p = 0.01$), and hematocrit (OR: 1.19; 95% CI: 1.01–1.40; $p = 0.04$) were independent predictors of severe sleep apnea. The National Institutes of Health Stroke Scale (NIHSS; OR: 1.30; 95% CI: 1.1–1.5; $p = 0.001$) and severe sleep apnea (OR: 9.7; 95% CI: 1.3–73.8; $p = 0.03$) were independently associated to mRS >2 at six months, after adjusting for confounders.

Conclusion: Patients with acute ischemic stroke in Brazil have a high frequency of SDB. Severe sleep apnea is associated with a poor long-term functional outcome following stroke in that population.

1. Introduction

Sleep-disordered breathing (SDB) and cerebrovascular disease (CVD) are highly prevalent worldwide [1,2]. Recent accumulating clinical and epidemiological evidences suggest a strong causal relationship between them [3–8]. Obstructive sleep apnea (OSA) is the most common form of SDB and it is characterized by repetitive episodes of partial or complete upper airway obstruction during sleep [9]. A population-based survey study in Brazil identified that around 32% of adults fulfill the criteria for OSA syndrome, according to the International Classification of Sleep Disorders – ICSD-2 [10]. This prevalence is dramatically greater than that reported in other epidemiological studies, which has been partly attributed to specific characteristics of the Brazilian population sample, including a higher proportion of elderly and obese [11].

Several studies have shown that OSA is very frequent in acute stroke patients and has been associated with poor short-term and long-term outcomes [12–15]. In addition, OSA has been identified as an independent risk factor for stroke [6–8]. In Brazil, CVD is the leading cause of death and disability, imposing a significant economic and social burden on society [16]. A better understanding of the factors that contribute to adverse outcome of stroke patients in developing countries could guide the search for appropriate interventions to change the course of this dramatic scenario. OSA is a treatable condition and therefore its treatment seems to be a potential target to improve the outcome for acute stroke patients [17–19]. Unfortunately, there is a lack of data about the relationship between SDB and stroke patients within the Brazilian

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population. Furthermore, the impact of SDB on functional outcome of stroke patients is still controversial [13,14,20].

We sought to analyze the prevalence and severity of SDB in acute ischemic stroke patients in Brazil; to identify clinical and laboratorial data related to the presence and severity of SDB; and to assess the relationship between sleep apnea and functional outcome six months after the cerebrovascular event.

2. Material and methods

2.1. Subjects

Patients with first-ever supratentorial ischemic stroke within 24 h of symptoms' onset were prospectively assessed at the Emergency Department of our University Hospital. Patients with age <18 or >80 years old; stupor or coma; severe chronic obstructive pulmonary disease; clinically decompensated congestive heart failure; baseline oxyhemoglobin saturation <92%; or recent myocardial infarction were excluded. Consecutive patients who fulfilled all the inclusion criteria and none of the exclusion criteria were screened for the present study. Either patients or their legal representative were approached for written informed consent and all agreed to participate. The study design was approved by our Institutional Review Board.

2.2. Data collection

Demographical data, vascular risk factors, presence of habitual snoring (three to four times a week or more), and the time of symptoms' onset were recorded. This information was given by the patients themselves or their relatives. Wake-up stroke was defined when the patient was normal before sleep and woke up with neurological deficits in the morning [21]. All patients were assessed with a neurologic examination that included the Glasgow Coma Scale (GCS) and the National Institutes of Health Stroke Scale (NIHSS), which version has been previously validated in Brazil [22]. Early neurological deterioration (END) was defined as an increase of at least four points in the NIHSS from baseline within 48 h of hospital admission [23]. Body mass index (BMI) was also registered. The degrees of functional recovery were assessed by the modified Rankin Scale (mRS) at 6 months after stroke onset [22]. The examiner was blind to the neurological clinical data of hospital admission, as well to the sleep study results.

Routine laboratory tests (complete blood cell count, biochemical profile, renal function) and brain computed tomography (CT) scan were performed on admission. The ischemic stroke subtype was classified according to Trial of Org 10172 in Acute Treatment (TOAST) study [24].

All subjects underwent a full polysomnography (PSG), the gold standard exam for SDB diagnosis. The PSG was performed within the first 24 h after symptoms' onset at the emergency unit, from 11:00 p.m. to 7:00 a.m., using a digital system (Sommeil S80 Meditron; Sao Paulo, BR or BioLogic Sleepscan II™; Mundelein, IL, USA). System parameters included six EEG channels (F3-A2, F4-A1, C3-A2, C4-A1, O1-A2, O2-A1), two electro-oculographic leads, chin and bilateral anterior tibialis surface electromyograms, body position sensor, electrocardiogram, snore sensor, thermopar (oronasal thermal airflow), nasal cannula, thoracic and abdominal gauges, and finger pulse oximetry. Sleep stages were scored according to standard criteria [25] by an experienced neurophysiologist who was blind to the neurological clinical data. Sleep apnea was defined by an AHI ≥ 10 and classified as obstructive or central according to the type of predominant event. Therefore, predominantly central sleep apnea was diagnosed when more than 50% of respiratory events were of the central type.

2.3. Statistical analysis

The means ± standard deviations (SD) or medians with interquartile ranges (IR) were calculated for numeric variables. Student *t*-test, Mann-Whitney *U*-test, Chi-square test or Fisher's exact test was used as appropriate on univariate analysis. Backward stepwise logistic regression analysis was used to identify the independent predictors of sleep apnea (AHI ≥ 10), severe sleep apnea (AHI ≥ 30), and poor functional outcome (mRS > 2) at six months. The independent contribution of variables with a p-value < 0.1 on univariate analysis was assessed. A p-value < 0.05 (two-sided) was used as the threshold for statistical significance. The data were analyzed using the SPSS statistical software package, version 20.0 (Chicago, IL, USA).

3. Results

Sixty-nine patients were enrolled in the present study. The first 29 patients had already been reported in a previous study with a different primary objective [26]. Since then, we were able to expand our sample to improve the power of our analysis. Among all subjects, 52 (75.4%) were men, and the mean age was 60.8 ± 11.8 years. Hypertension was the most frequent risk factor for stroke (71%). History of habitual snoring was retrieved from 51 (73.9%) patients and the mean BMI was 26.3 ± 4.5 kg/m^2. Eighteen (26.1%) patients had wake-up stroke. The median NIHSS was 11 (IR: 6–18) and the median GCS was 14 (IR: 12–15) on admission. Only four (5.8%) patients fulfilled the criterion for END. Twenty-two (31.9%) patients underwent thrombolytic treatment with t-PA according to our institutional protocol (Table 1).

Concerning the laboratory tests on admission, the mean serum glucose was 128.2 ± 53.2 mg/dL, hemoglobin was 14.6 ± 1.8 g/dL, hematocrit level was 44.3 ± 5.4 and platelet count was 223.9 ± 71.7 × 10^3 platelets/mL. Two male patients presented hematocrit value compatible with polycythemia (greater than 54%). All blood tests are summarized in Table 1.

An overnight PSG study was obtained for all subjects. The mean total time recorded was 425.1 ± 81.8 min and the mean total sleep time was 270 ± 105.6 min. No significant difference was observed in sleep efficiency between the apneic and the nonapneic groups. Time spent in stage N1 and stage N3 was significantly different between patients with sleep apnea and those without apnea. The mean AHI was 37.7 ± 30.2. Fifty-three patients (76.8%) exhibited AHI ≥ 10, and thirty-three (47.8%) presented severe sleep apnea (AHI ≥ 30). The majority of SDB (90.6%) was primarily OSA. Only five (9.4%) patients exhibited predominantly central apnea. The mean O_2 saturation and the mean percentage of time with hemoglobin saturation <90% (CT90) were 93.6 ± 2.3 and 10.7 ± 16.6, respectively, with significant difference between nonapneics and apneics group (Table 2).

Age (p = 0.003), habitual snoring (p = 0.02), hemoglobin (p = 0.02), hematocrit (p = 0.02), and platelet count (p = 0.009) were significantly different between those with AHI ≥ 10 and AHI < 10. On a multivariate analysis, age (OR: 1.09; 95% CI: 1.03–1.15; p = 0.004) and hematocrit (OR: 1.18; 95% CI: 1.03–1.34; p = 0.01) were independently associated with sleep apnea (AHI ≥ 10). In addition, age (OR: 1.13; 95% CI: 1.03–1.24; p = 0.01), BMI (OR: 1.54; 95% CI: 1.54–2.18; p = 0.01) and hematocrit (OR: 1.19; 95% CI: 1.01–1.40; p = 0.04) were independently associated with severe apnea (AHI ≥ 30) (Table 3).

Regarding the TOAST classification, 29 (42%) patients were classified as cardioembolic stroke, 12 (17.4%) as atherothrombotic stroke, 11 (15.9%) as small-vessel disease, one (1.4%) as other causes, and 16 (23.2%) as undetermined etiology. A cardioembolic etiology was more commonly diagnosed in patients with AHI ≥ 10. However, there was no significant difference in severity and etiology of stroke between groups with and without sleep apnea (Table 1).