Prevalence and Predictors of Upper Airway Obstruction in the First 24 Hours After Acute Stroke

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Background and Purpose—The prevalence of sleep-disordered breathing after stroke has been reported to be between 32% and 71%. However, the first 24-hour period, when upper airway obstruction may have a critical effect on the cerebral circulation because of hemodynamic fluctuations and repetitive hypoxia, has not been studied. Furthermore, data on prediction of upper airway obstruction after stroke are limited. This study sought to assess the prevalence of upper airway obstruction in the first 24 hours of stroke and to ascertain whether its occurrence could be predicted.

Methods—One hundred twenty patients with acute stroke underwent a respiratory variable-only sleep study, started within 24 hours of onset of neurological symptoms. Sleep history and stroke characteristics were recorded on admission.

Results—We found that 79%, 61%, and 45% of the patients had a respiratory disturbance index greater than 5, 10, and 15 events per hour, respectively. Patients had a significantly higher respiratory disturbance index when nursed in the supine (29 events per hour), supine left (29 events per hour), and supine right (24 events per hour) positions than in any other position (P<0.0001). On logistic regression analysis, BMI (P=0.025), neck circumference (P=0.026), and limb weakness (P=0.025) independently predicted the occurrence of upper airway obstruction in the first 24 hours after acute stroke.

Conclusions—Upper airway obstruction is common in the first 24 hours after stroke, especially if patients are nursed in the supine position, and typical obstructive sleep apnea risk factors (body mass index and neck circumference) appear to be the best predictors of its occurrence. Stroke characteristics (severity, clinical subtype, and clinically assessed pharyngeal function) are not independently associated with upper airway obstruction after stroke. (Stroke. 2002;33: 2037-2042.)

Key Words: prevalence ■ sleep apnea syndromes ■ stroke, acute

Obstructive sleep apnea (OSA) and snoring are common conditions. The prevalence of sleep-disordered breathing (SDB) in a middle-aged population has been reported to be 24% in men and 9% in women. There is evidence to suggest that OSA and snoring may be independent risk factors for stroke, although this has been disputed. The repeated upper airway obstruction in patients with OSA occurs as a consequence of a reduction in pharyngeal muscle tone during sleep. The pharyngeal muscles may be affected in stroke; neurological dysphagia has been demonstrated in 30% to 40% of patients admitted to the hospital with unilateral hemispheric stroke. Impaired consciousness during stroke or positioning to avoid pressure sores may further compromise airway function. Therefore, stroke or its treatment could cause OSA to develop de novo or worsen existing OSA.

Recently, interest has grown in the occurrence of SDB, and in particular OSA, after stroke. Several studies have reported that up to 71% of patients with stroke may have SDB. However, none of these studies examined the first 24-hour period, when SDB may have a harmful effect on critically ischemic brain tissue through the repeated hemodynamic oscillations or episodes of hypoxia that are known to accompany occlusion of the upper airway in patients without stroke; systemic blood pressure, pulse rate, and cardiac output all decrease during an obstructive apnea and increase suddenly at apnea termination. Cerebral blood flow also decreases with upper airway obstruction. Previous studies have reported that up to 43% of stroke patients will have a progression of their neurological deficit. This typically occurs early after stroke onset, with 87% occurring within the first 48 hours.

There is no evidence regarding whether those patients who develop SDB in the acute phase of stroke can be predicted and, in particular, whether traditional OSA risk factors or stroke characteristics are the most predictive. Increasing age, male sex, previous history of snoring, witnessed apneas, body mass index (BMI), and neck circumference have previously been demonstrated to be risk factors for OSA. If upper airway obstruction is indeed common during sleep in the first 24 hours of stroke, inter-
ventions targeted to abolish SDB (eg, continuous positive airway pressure [CPAP]) may improve outcome, although, as pointed out by Culebras, formal clinical trials are needed. Since CPAP may be difficult to tolerate, particularly in the elderly, it is important to identify those most likely to benefit. The aim of this study was to ascertain the prevalence and severity of upper airway obstruction occurring during sleep in the first 24 hours in patients admitted to the hospital with stroke and to determine whether its occurrence can be predicted.

Subjects and Methods

Subjects

One hundred forty-seven patients admitted to 1 of 3 wards in the Leeds Teaching Hospitals National Health Service Trust who had suffered a stroke in the previous 24 hours were asked to participate. Although stroke patients were admitted to other wards during the recruitment period, they were excluded because stroke admissions to these wards were not frequent enough to ensure that nursing staff maintained their familiarity with the equipment used. Written consent was obtained from either the patient or, if they were unable, their next of kin. Consent was sought as soon as possible after admission to the ward, and the studies were started directly thereafter. Twenty-seven patients either declined to give consent or were unable to tolerate the monitoring equipment, leaving 120 patients in the study. All patients admitted to the Leeds Teaching Hospitals National Health Service Trust with stroke are registered on a database. Therefore, we were able to determine whether the basic demographics of the sample studied were representative of all stroke patients admitted to the hospital during the study period. The study was approved by the local ethics committee.

Patient Assessments

Strokes were classified into the 4 Oxford Community Stroke Project (OCSP) clinical subtypes (total anterior circulation syndromes [TACS], partial anterior circulation syndromes [PACS], lacunar syndromes [LACS], and posterior circulation syndromes [POCS]). Stroke severity was graded with the use of the Scandinavian Stroke Scale, Glasgow Coma Scale and limb weakness (Motricity Index) were documented on admission. Disability and handicap were assessed on admission with the use of the Barthel Index and the modified Rankin Scale, respectively. Pharyngeal function was assessed by examining cough quality, palatal elevation, and presence or absence of pharyngeal sensation on recruitment to the study and on the second and third days after admission. Swallowing was also assessed, when possible, by asking patients to swallow 10 mL of clear fluid from a container (the patients sat upright and were supported and helped to hold the container if necessary). Any coughing or choking after swallowing some fluid, drooling, or pooling of fluid in the mouth was taken to indicate an unsafe swallow. Patients with a decreased level of consciousness (Glasgow Coma Scale <8) were not subjected to the swallowing test and were assumed to have an unsafe swallow. Each patient had a CT brain scan performed by 72 hours to confirm the diagnosis and pathological type of stroke. Previous history of stroke was documented (if patients or their relatives recalled a prior event or a previous admission with stroke had been documented in the medical notes). Age, sex, previous history of snoring, BMI, and neck circumference were all recorded. Daytime sleepiness before stroke was estimated with the use of the Epworth Sleepiness Scale.

Sleep Studies

Studies were performed with the use of the Alice 4 sleep system (Respiroline) and were started as soon as possible after admission and continued up to a total of 24 hours or until patients requested that the equipment be removed (each patient had at least 6 hours of data recorded during the night). Nasal airflow, thoracoabdominal effort, heart rate (ECG), oxygen saturation (finger probe), abdominal and respiratory effort (strain gauge), snoring (microphone), body position (sensor detecting 8 points of compass on thoracic strain gauge), and light intensity (light meter) were recorded. Patients who were unable to tolerate full monitoring during the day (either because of being ambulatory or agitated) were studied with the use of pulse oximetry (Pulse Ox 3i, Stowood Scientific Instruments) only for that period, but all were studied with the Alice 4 system at night. Each patient was studied in his or her own hospital bed and was not transported to the sleep laboratory. Usual nursing and physiotherapy practices were not altered during the study; in particular, the patient was positioned according to the usual ward protocol. Ward staff members were not able to access raw data during the study. The Alice 4 monitor displayed a “channel failed” message on the screen if the signal from any channel became inadequate. Nursing staff checked the equipment on an hourly basis and repositioned any sensors that had become disconnected. Each study was individually scored by the same physician (P.M.T.) using standard criteria. Respiratory disturbance index (RDI) was subsequently calculated as the number of apneas and hypopneas per hour of study.

Definitions

An apnea was defined as a cessation in airflow of ≥10 seconds and was classified as obstructive if there was maintenance of thoracic or abdominal effort, central if there was no thoracic or abdominal effort, or mixed if there was a combination of the 2. A hypopnea was defined as 50% reduction in airflow associated with a 4% oxygen desaturation. Cheyne-Stokes respiration was defined as central apnea or hypopnea alternating with hyperpnea in a crescendo-decrescendo pattern.

Analysis of Data

Statistical analysis of all data was performed with SPSS version 9.0 for Windows. Patient demographic data and sleep study data are expressed as mean and SD. Ordinal data derived from various scales used are described as median and interquartile range (IQR). Statistical comparisons were made with the use of Student’s t tests, chi-square tests, and Mann-Whitney U tests where appropriate. Logistic regression analysis was used to determine whether upper airway obstruction in the first 24 hours after stroke could be predicted from traditional OSA risk factors and stroke characteristics and severity. A probability value of <0.05 was considered to indicate statistical significance.

Results

All patients enrolled in the study had the diagnosis of stroke confirmed clinically and radiologically. Table 1 shows the demographics of our study population. There are no significant age or sex differences between the study population and all patients admitted with stroke to the hospital in Leeds. A history of snoring was found in 25.8% of our patients, and 4.2% reported previous witnessed apneic events. The median Epworth score on admission was 6 (IQR, 4 to 9). Table 2
TABLE 2. Stroke Characteristics

<table>
<thead>
<tr>
<th>Stroke Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Scandinavian Stroke Scale, median (IQR)</td>
<td>30 (16.25–42.75)</td>
</tr>
<tr>
<td>Glasgow Coma Scale, median (IQR)</td>
<td>15 (12–15)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>35.8%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>16.7%</td>
</tr>
<tr>
<td>First stroke</td>
<td>73.3%</td>
</tr>
<tr>
<td>TACS</td>
<td>44%</td>
</tr>
<tr>
<td>PACS</td>
<td>26%</td>
</tr>
<tr>
<td>POCS</td>
<td>7%</td>
</tr>
<tr>
<td>LACS</td>
<td>23%</td>
</tr>
</tbody>
</table>

The mean delay from estimated time of onset of symptoms until the start of the sleep study was 10 hours 50 minutes. For patients who awoke with their stroke, estimated time of onset of symptoms was taken as 5 AM. Patients took an average of 3 hours 58 minutes to present to the accident and emergency department after their stroke and spent an average of 3 hours 54 minutes before being transferred to a ward. The mean (SD) length of studies was 733 (330) minutes. Figure 1 shows the proportion of SDB, expressed as RDI, in the study group; 60.8% of the stroke patients had an RDI of >10 events per hour (mean [SD] RDI, 17.3 [13.1]). The majority of patients had upper airway obstruction as their main form of SDB. Only 9% had more central than obstructive sleep apnea. However, 38% of patients had Cheyne-Stokes respiration at some stage during their study, but only 12% spent >10% of the study in Cheyne-Stokes respiration. We found a median of 37 (IQR, 8 to 100) obstructive apneas per study, and patients spent a median of 3.5% (IQR, 1.6 to 6.9) of their study period in obstructive apnea. The upper airway obstruction was significantly more severe when patients were nursed in the supine (S) (P<0.0001), supine left (SL, P<0.005), and supine right (SR, P<0.03) positions than in any other position. Patients spent significant periods of time in each position, ranging from a mean of 35 minutes prone to 333 minutes supine. Table 4 shows the oxygen saturation and snoring data.

Logistic regression analysis was used to identify factors that would predict those stroke patients who would develop upper airway obstruction (RDI >10) in the first 24 hours. Typical OSA-type risk factors and stroke characteristics were entered into the equation. Table 5 shows the regression coefficients, Wald statistics, significance, odds ratios, and 95% CIs of the significant predictors. Typical OSA-type risk factors such as BMI (P<0.025) and neck circumference (P<0.026) appear to be the best predictors of the development of upper airway obstruction. Limb weakness (P<0.025) is also an independent predictor; however, other stroke characteristics, such as severity and subtype, and prior history of stroke do not appear to influence the development of upper airway obstruction.

Discussion

This study demonstrates that upper airway obstruction is common in the first 24 hours after stroke. The majority of patients had obstructive apneas (median, 37 per study) as opposed to central apneas (median, 3 per study) or Cheyne-Stokes respiration as their primary breathing disturbance. No matter how it was defined (RDI >5, >10, >15, or >20 events per hour), a significant proportion of patients had SDB, with 61% having RDI of >10 events per hour. During this study data were recorded for up to 24 hours; therefore, because total sleep time was not recorded and total length of study was used as the denominator when RDI was calculated, the indices calculated will be an underestimate of the degree of SDB after stroke. The observation that the severity of the upper airway obstruction after stroke was significantly worse in the supine position has not been previously reported. However, it is accepted that patients with OSA often experience more frequent apneas in the supine position. This suggests that careful positioning of patients may significantly reduce the severity of SDB after acute stroke. Measures of obesity were the best predictors of upper airway obstruction after stroke. There was also an association between upper
al9 performed pulse oximetry on a group of 47 stroke patients and found that 77% and 62.5% of patients, respectively, had RDI mean of 16 and 9 days after the event, respectively. They transient ischemic attack, with full polysomnography, at a median of 13 days after stroke and found that 32% had a 4% oxygen desaturation index of >10 per hour. Our study demonstrates a prevalence of upper airway obstruction similar to that found in previous studies. However, as far as we are aware, this is the only study that focuses on the first 24 hours after the onset of stroke. This is a crucial observation because this is when the physiological consequences of repeated upper airway obstruction might have the most impact on critically ischemic but viable brain tissue. Several hemodynamic oscillations are known to occur during obstruction of the upper airway. Blood pressure decreases to a nadir at the midpoint of the apnea because of the increasingly negative intrathoracic pressures generated by repeated respiratory efforts against an obstructed pharynx. Blood pressure will then rise gradually until apnea termination, when there will be an overshoot, thought to be due to resumption of respiration with arousal.13,45 During obstructive apnea, episodes of bradycardia14 and occasionally heart block have been reported,46 and cardiac output can decrease by up to one third.15 At apnea termination, tachycardia16 and increases in cardiac output of up to 20% are seen.15 Episodic reductions in cerebral blood flow, measured by transcranial Doppler, during upper airway obstruction have also been reported in patients with OSA.17 The combination of these hemodynamic fluctuations, together with repeated episodes of hypoxia, may contribute to the ischemic brain insult.

We did not perform full polysomnography because some patients found even the limited monitoring equipment that we used intrusive; the additional requirement for scalp electrodes and their connecting wires may have reduced the number of patients able to tolerate the studies. Second, conventional sleep staging was developed in normal subjects, and the interpretation of the electroencephalographic (EEG) signal in patients with cortical damage due to stroke may not be valid. Furthermore, Douglas et al48 showed in 200 consecutive polysomnographic studies that the addition of an EEG did not affect the diagnosis of OSA. They showed that the use of respiratory variable-only monitoring was more accurate than pulse oximetry and allowed characterization of apneas into obstructive, central, or mixed. This is particularly important in patients with stroke, who may have Cheyne-Stokes respiration. Because the denominator for the calculation of the RDI was total study time rather than total sleep time, our estimate of the incidence of upper airway obstruction is likely to be an underestimate. The study of Douglas et al,48 however, suggests that this is unlikely to have a significant effect on the diagnostic classification. However, a limitation of nonuse of the EEG is that rapid eye movement (REM) sleep, when OSA and oxygen desaturation would be expected to be most severe, could not be demonstrated accurately. Damage to the ischemic penumbra after acute stroke may be worst during this period.

Parra et al12 recently published results of a study in which they used a similar technique of respiratory variable-only monitoring to examine 161 patients with stroke or transient ischemic attack between 48 and 72 hours after the cerebrovascular event. Again, the crucial immediate poststroke period was not studied, and although the amount of SDB appears similar to our study (71.4% with RDI >10), there were significant differences in the type of events recorded: 38.5% and 26.1% of the patients exhibited predominantly central apneas and Cheyne-Stokes respiration for >10% of the night, respectively, compared with only 9% and 12% of our patients. The reason for this difference is not easily explained, but the stroke severity appears to be less than in our study; only 5% were dead at 3 months (25% of our patients died in the hospital), and 25% of those studied had a transient ischemic attack and presumably would have had no neurological symptoms at the time of their sleep study.

A significant number of patients were excluded from the study because they did not arrive on the designated ward until after 24 hours had elapsed, usually because of time spent waiting in an assessment unit. This is an important issue,
especially if treatment of SDB in the first 24 hours of stroke, for instance with CPAP, is to be considered. However, we were able to confirm that the basic demographics of our sample were representative of all patients admitted to hospital in Leeds with stroke. Previous studies\textsuperscript{9,10,12} have not ensured that patients were a representative sample; in particular, the group of stroke patients studied by Bassetti and Aldrich\textsuperscript{11} was younger (mean [SD] age, 59 [15] years) than one would usually expect.

The finding that typical OSA-type risk factors have more influence than stroke characteristics in predicting patients who have upper airway obstruction after stroke was not surprising. Other studies have shown that stroke patients with RDI $\geq 20$ have a large neck circumference,\textsuperscript{49} while others have also demonstrated no link with stroke subtype or location.\textsuperscript{10,12} The finding that there was no correlation between the occurrence of upper airway obstruction and stroke severity (as measured by the Scandinavian Stroke Scale) and clinical stroke subtype was not previously reported. These are important observations and argue against the theory that SDB is just a marker of severe stroke.

This study addresses several important issues. First, it confirms that SDB is common in the acute phase of stroke and that the majority of the respiratory disturbances seen are due to obstruction of the upper airway. The majority of the SDB occurred when the patients were supine, suggesting that careful positioning of the patients may be important in its prevention. Second, stroke patients who demonstrate upper airway obstruction are predisposed by their body habitus. Third, stroke subtype and severity have little influence, and therefore upper airway obstruction will be seen in a wide range of stroke patients.

Further investigation of the effect of upper airway obstruction in the first 24 hours of stroke is required. The known physiological changes that occur with OSA, such as blood pressure variability and altered cerebral blood flow, could have profound effects on the ischemic penumbra. The effect this may have on early neurological deterioration, mortality, or recovery of functional status and whether new therapies in stroke, targeted at preventing upper airway obstruction (eg, CPAP or patient positioning), may alleviate these effects remain important unanswered questions. In particular, additional data are needed about the relationship between respiratory events and hemodynamic fluctuations in acute stroke and whether other factors, such as length of apnea and depth of oxygen desaturation, are more important than number of events in determining outcome.

**Acknowledgement**

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**References**

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