Unexpected Nocturnal Hypoxia in Patients With Acute Stroke

Christine Roffe, MD; Sheila Sills, RGN; Mohamed Halim, MSc; Kathryn Wilde, PhD; Martin B. Allen, MD; Peter W. Jones, PhD; Peter Crome, MD

Background and Purpose—Patients who have had a stroke are at risk of hypoxia through alterations in the central regulation of respiration, through aspiration, and through respiratory muscle weakness. Sleep-related breathing disorders are common and may lead to episodes of nocturnal hypoxia even when daytime oxygenation is normal. The aim of this study was to assess the prevalence of unexpected nocturnal hypoxia in stroke patients.

Methods—Consecutive adult patients with stroke were recruited within 72 hours of admission to hospital. Patients with indications for oxygen treatment were excluded. Older adults from the local community were recruited as control subjects. Oxygenation was assessed by pulse oximetry (Minolta 3i) for 5 minutes when awake before bedtime and continuously from 11 PM until 7 AM.

Results—Of the 238 potentially eligible stroke patients, 120 were excluded because they required oxygen, 118 were recruited, and 100 had adequate pulse oximetry data. The mean ± SD age was 74 ± 8 years for stroke patients and 72 ± 8 years for control subjects (n = 85). Mean awake oxygen saturation (SO2) was 94.5 ± 1.7% for the stroke group and 95.8 ± 1.7% for the control group (P < 0.001). Mean nocturnal SO2 was 93.5 ± 1.9% in stroke patients and 94.3 ± 1.9% in control subjects (P < 0.01). Stroke patients had a higher oxygen desaturation index (ODI 4%) (8.9 versus 2.1, P < 0.001). In addition, 23% of stroke patients spent >30 minutes with SO2 <90% during the night.

Conclusions—Oxygen saturation at night is ~1% lower than when awake. Almost a quarter of stroke patients who were normoxic at screening during the day spend >30 minutes with an oxygen saturation <90%. (Stroke. 2003;34:2641-2645.)

Key Words: hypoxia ■ oximetry ■ oxygen ■ stroke ■ stroke, acute

Hypoxia during the first few days after a stroke may affect cells in the ischemic penumbra adversely and lead to worsening of the neurological deficit and clinical outcome.1 Patients with acute stroke are at risk of developing hypoxia for a number of different reasons. These include stroke-related factors such as alterations in the central regulation of respiration,2 sleep apnea,3,4 and weakness of the respiratory muscles on the hemiplegic side.5,6 Complications of the stroke such as aspiration,7,8 chest infections,9,10 and pulmonary embolus9,10 may further impair oxygenation. Additionally, preexisting pulmonary and cardiovascular problems may predispose to the development of hypoxia. An observational study has shown that >60% of patients develop hypoxia within the first 60 hours after stroke.11

Although routine oxygen supplementation in all patients with acute stroke cannot be recommended in the light of current evidence,12 there is general consensus that hypoxia after acute stroke should be treated.13-15 Assessment of oxygenation is routine on admission of a stroke patient, but once normal oxygen saturation is confirmed, further monitoring of oxygenation may not be deemed necessary.

Sleep-related breathing disorders have been reported in 44% to 95% of stroke patients3,16-19 and may cause nocturnal hypoxia in patients who appear normoxic during the day. Nocturnal hypoxia can easily be missed by clinical assessment in patients who are asleep and do not complain of any symptoms. In the presence of low lighting, as is usual during sleep, cyanosis is unlikely to be noticed.

In this study, we assessed the prevalence of unexpected nocturnal hypoxia in patients with acute stroke who were normoxic on presentation and had no definite indications for oxygen supplementation.

Subjects and Methods

This prospective observational study of nocturnal oxygen saturation in the acute phase after stroke was conducted from December 1998 through March 2001. Consecutive adult patients with a clinical diagnosis of acute stroke were recruited within 72 hours of admission. Subjects were recruited by a researcher working part time (Monday through Thursday). The study setting was a large district general hospital (City General Hospital, Stoke-on-Trent, North Staffordshire, UK). The hospital serves an unsedected, mainly urban population of 450 000 inhabitants. Patients in whom the initial diagnosis of stroke was not confirmed, patients with severe persistent disability from a prior stroke, those who were too confused or too restless to retain the finger probe in place or had reduced peripheral perfusion leading to an unobtainable or poor oximetry trace, pregnant women, and subjects who were moribund or refused consent...
were excluded from the study. Patients with definite indications for oxygen supplementation (oxygen saturation $\leq 90\%$, decompensated congestive cardiac failure, pneumonia with consolidation on the chest x-ray, known chronic hypoxia requiring long-term oxygen treatment) and patients for whom the admitting physician had prescribed oxygen treatment to be given continuously were excluded.

**Control Subjects**

The control group was designed to be as close as possible to the stroke patients in age, social background, and comorbidity. Therefore, patients’ spouses were recruited as control subjects whenever possible. Otherwise, older adults from the same local community, mainly patients’ friends and other hospital visitors, were recruited.

**Consent**

Written informed consent was sought from all study participants. Assent from the next of kin was accepted if the patient was unable to give fully informed consent.

**Clinical Assessments**

Baseline clinical assessments included age, sex, height, weight, smoking status, prescribed medications, a history of snoring, and known medical problems. Body mass index was calculated for each subject. All strokes were classified by clinical criteria as total anterior circulation syndrome (TAC), partial anterior circulation syndrome (PAC), lacunar syndrome (LAC), and posterior circulation syndrome (POC) by use of the Oxfordshire Community Project Classification. Stroke origin was determined by CT of the head and reported as cerebral infarct or intracerebral hemorrhage. Hemorrhagic infarcts were recorded as infarcts.

**Oximetry**

Pulse oximetry was performed overnight starting on the day of recruitment. Hands were inspected to ensure that the fingers were warm and well perfused. Nail polish was removed, and long fingernails were clipped when necessary. Pulse oximeters (Pulsox-3i, Minolta, Stowood Scientific Instruments) were attached to the wrist, and the sensory probes were fitted to the index finger. To reduce movement artifact, the hemiparetic side was used for oximetry. The oximeter was placed at 9 PM and removed at 9 the next morning. The mean oxygen saturation during the first 5 minutes after probe placement was recorded as the baseline awake reading. Oximetry results between 11PM and 7 AM were defined as nocturnal readings. It is assumed that most patients were asleep during this time. Movement artifact (restlessness, trips to the toilet, etc) and snoring were recorded in a diary by the night nurse. Probes that were displaced accidentally during the night were replaced as soon as possible.

After completion of the recording, data were downloaded onto a personal computer with Oximeter Download Software for Windows (Stowood Scientific Instruments). Recordings with data for <4 hours were not included in the final analysis. Values for oxygen saturation ($SO_2$) were obtained by performing a moving average for the last 5 seconds, updated every second. Desaturations (ODI 4%) were defined as a 4% fall in saturation from baseline just before the drop. Because some of the recordings were for <8 hours because of probe displacement, results for T90 (the time the subjects spent with an $SO_2<$90%) were corrected to a notional 8-hour period with this formula: T90, (in minutes) = (T90 in minutes/actual recording time in minutes) x 480.

**Capillary Blood Gases**

Capillary blood gases were obtained from the ear lobe in stroke patients in the morning after overnight pulse oximetry after local application of a rubefacient (Transvasin cream) to the pinna.  

### TABLE 1. Baseline Characteristics of the Study Population

<table>
<thead>
<tr>
<th>Demographic descriptors</th>
<th>Control Subjects (n=85)</th>
<th>Acute Stroke Patients (n=100)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean±SD), y</td>
<td>72±8</td>
<td>74±8</td>
<td>NS*</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>44</td>
<td>46</td>
<td>NS†</td>
</tr>
<tr>
<td>Body mass index (mean±SD), kg/m²</td>
<td>25±4</td>
<td>27±6</td>
<td>NS*</td>
</tr>
<tr>
<td>Smokers, %</td>
<td>13</td>
<td>24</td>
<td>NS†</td>
</tr>
<tr>
<td>Snorers, %</td>
<td>41</td>
<td>49</td>
<td>NS†</td>
</tr>
<tr>
<td>Concomitant medical problems, %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertension</td>
<td>22</td>
<td>61</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1</td>
<td>19</td>
<td>&lt;0.001†</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>13</td>
<td>28</td>
<td>&lt;0.01†</td>
</tr>
<tr>
<td>Congestive cardiac failure</td>
<td>0</td>
<td>5</td>
<td>&lt;0.05†</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>6</td>
<td>17</td>
<td>&lt;0.05†</td>
</tr>
<tr>
<td>Chronic obstructive pulmonary disease</td>
<td>17</td>
<td>15</td>
<td>NS†</td>
</tr>
</tbody>
</table>

Shown are baseline characteristics of stroke patients and control subjects included in the study. Statistical comparisons were made with t tests for continuous data, * $\chi^2$ tests, † and Fisher’s exact tests for categorical data.

**Statistical Analysis**

Descriptive statistics were calculated with Microsoft Excel for Office 2000. Statistical tests were conducted with SPSS, version 10, for Windows. Approximately normally distributed data are given as mean±SD. Medians and ranges were used to describe nonnormally distributed data. Statistical comparisons were made with t tests, $\chi^2$ tests, or Mann-Whitney tests when appropriate (specific tests used for each comparison are given in Results and the tables).

**Results**

**Exclusions and Dropouts**

During the recruitment period, 1363 patients with acute stroke were recorded by the research nurse. Of those, 825 were excluded because >72 hours had passed since their stroke, 120 had persistent neurological deficit from a prior stroke, 3 were too restless to tolerate the probe, 1 was pregnant, 63 did not provide consent or assent, 44 were moribund, and 69 were admitted under the care of 2 physicians who did not take part in the study. Of the remaining 238 stroke patients potentially recruitable to the study, 51 were excluded because continuous oxygen treatment had been prescribed by the admitting doctor; 69 other stroke patients were excluded because they had clinical indications for oxygen treatment. Thus, 118 stroke patients matched the inclusion criteria and were recruited for the study. In 13, oximetry was not successful (no data), and 5 had inadequate data. One hundred patients had adequate data and were included in the analysis.

**Baseline Characteristics**

Baseline characteristics of stroke patients and community control subjects are shown in Table 1. The 2 groups were well matched for age, sex, and body mass index. The prevalence of hypertension, atrial fibrillation, ischemic heart disease, and
diabetes was significantly higher in the stroke group. Within the stroke group, there were 18% TAC, 32% PAC, 42% LAC, 5% POC, and 3% transient ischemic attacks. Eighty-eight percent were cerebral infarcts; 5% were primary intracerebral hemorrhages; and in 7%, the cause was not known (5 patients died before a CT of the head could be arranged).

Results of the Pulse Oximetry

Results of the pulse oximetry for stroke patients and control subjects are shown in Table 2. Baseline awake oxygen saturation was at 94.5%, which was 1.3% lower than in nonstroke controls. Mean nocturnal oxygen saturation was 1% lower than the baseline awake daytime oxygen saturation in both the stroke and control groups \((P<0.001\) and \(P<0.01\), respectively; Student’s \(t\) tests). Stroke patients also had significantly more 4% desaturations than controls \((P<0.001\), Mann-Whitney test). Fifty-two percent of stroke patients spent >5 minutes, 41% spent >10 minutes, 23% spent >30 minutes, and 15% spent >1 hour with an oxygen saturation of <90% \(\left(T_{90}\right)\).

When nocturnal oxygen saturation was examined in relation to stroke classification (TAC, PAC, LAC, and POC), no consistent pattern emerged. Mean \(\pm\)SD nocturnal oxygen saturation was 92.5\(\pm\)2.2, 93.5\(\pm\)1.4, 93.8\(\pm\)1.2, and 93.8\(\pm\)1.2, respectively, for each stroke type, with the lowest oxygen saturation in TAC patients. The oxygen desaturation index was higher in patients with LAC (5.3) than in those with TAC (3.9), PAC (3.4), or POC (2.9).

Capillary Blood Gases

Capillary blood gases were obtained from 58 of the 100 stroke patients. Reasons for not obtaining capillary blood gases were as follows: capillary blood gas analyser not available \((n=30)\), no comment \((n=4)\), refusal of consent \((n=1)\), and inadequate sample \((n=7)\). Results are shown in the Figure and summarized in Table 3. Two patients \((4\%)\) had acidosis (both metabolic), 1 resulting from pulmonary emboli \((\text{pH } 7.21; \text{PCO}_2, 2.2 \text{kPa}; \text{PO}_2, 8.6 \text{kPa}; \text{HCO}_3, 10.8 \text{mmol/L})\) and 1 caused by heart failure \((\text{pH } 7.29; \text{PCO}_2, 4.8 \text{kPa}; \text{PO}_2, 9.3 \text{kPa}; \text{HCO}_3, 17.2 \text{mmol/L})\). Both fit the inclusion criteria but deteriorated between inclusion and collection of the blood gas sample. Twenty-four patients \((41\%)\) had a pH within the normal range \((7.37\text{ to } 7.45)\). Most patients \((n=32, 55\%)\) had a mild respiratory alkalosis \((\text{pH } 7.46\text{ to } 7.51)\). None of the patients with alkalosis had hyperoxia; most had a low or low-normal oxygen saturation \((\text{mean, } 9.4 \text{kPa}; \text{range, } 7.9\text{ to } 12.8 \text{kPa})\) with low-normal \(\text{PCO}_2\) \((\text{mean, } 4.3 \text{kPa}; \text{range, } 3.3\text{ to } 5.2 \text{kPa})\) and normal \(\text{HCO}_3\) \((\text{mean, } 26 \text{ mmol/L}; \text{range, } 23\text{ to } 29 \text{ mmol/L})\). Only 3 had a \(\text{PO}_2 >12 \text{kPa}\) \((\text{range, } 12.1\text{ to } 12.8 \text{kPa})\); all the others were <12 kPa.

Discussion

The aim of the study was to estimate the prevalence of nocturnal hypoxia in stroke patients who are not hypoxic when screened during the day. In both stroke patients and community control subjects, mean nocturnal oxygen saturation was \(\approx1\%\) lower at night than at baseline when awake. Both baseline awake and mean nocturnal oxygen saturation were \(\approx1\%\) lower in stroke patients than in community control subjects. The mean awake oxygen saturation for control subjects was just above the lower margin of the normal reference range \((95.0\% \text{ to } 98.5\%)\); for stroke patients, the mean was 94.5\%, just below the normal range. Thirty-two percent of stroke patients had a mean nocturnal oxygen saturation <93\%, and 6\% had a mean nocturnal oxygen saturation <90\%. These results underestimate the total hypoxic burden in unselected stroke patients because subjects who required oxygen at study entry were excluded. Because we did not assess oxygen saturation continuously during the day, we cannot exclude that patients had daytime desaturations in addition to the reported nocturnal hypoxia.

Stroke patients in this study were well matched to the community control subjects for age, sex, and body mass index. As was to be expected from the known risk factors for stroke, there were more smokers and more subjects with hypertension, atrial fibrillation, ischemic heart disease, and diabetes in the stroke group than among the control subjects. Considering the S-shaped relation between arterial oxygen tension and oxygen saturation, small decreases in oxygen ten-

<table>
<thead>
<tr>
<th>TABLE 2. Results of the Pulse Oximetry</th>
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<tr>
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<tr>
<td>Control Subjects</td>
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<td></td>
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<tr>
<td>Baseline (\text{SO}_2) (mean(\pm)SD), %</td>
</tr>
<tr>
<td>(\text{SO}_2) mean (mean(\pm)SD), %</td>
</tr>
<tr>
<td>(\text{SO}_2) mean &lt;90%, n (%)</td>
</tr>
<tr>
<td>(\text{SO}_2) mean &lt;93%, n (%)</td>
</tr>
<tr>
<td>(\text{SO}_2) min (mean(\pm)SD), %</td>
</tr>
<tr>
<td>ODI 4%, median (range), n</td>
</tr>
<tr>
<td>(T_{90c}) &lt;90%, median (range), min</td>
</tr>
<tr>
<td>(T_{80c}) &lt;80%, median (range), min</td>
</tr>
</tbody>
</table>

Continuous pulse oximetry was performed between 9 PM and 9 AM. Baseline \(\text{SO}_2\) represents the average of the first 5 minutes of the analysis while the subject was awake. Nocturnal results measurements were taken from 11 PM to 7 AM. These include \(\text{SO}_2\) mean (mean nocturnal \(\text{SO}_2\)), \(\text{SO}_2\) min (lowest nocturnal \(\text{SO}_2\)), ODI 4\% (oxygen desaturation index, e.g., number of 4\% dips per hour overnight), and \(T_{90c}\) and \(T_{80c}\) (analysis time spent with \(\text{SO}_2\) <90\% and <80\%, respectively, normalized for 8 hours). For nonnormally distributed data, medians and ranges are given.

*Student’s \(t\)-test; †\(\chi^2\) test; ‡Mann-Whitney test.
Results of capillary blood gases sorted by pH. Each number on the x axis represents 1 patient and is the same in all 4 panels. Normal ranges are shaded in gray. The majority of stroke patients have a mild respiratory alkalosis with high-normal or elevated pH, low-normal carbon dioxide tension (pCO₂), an oxygen tension (pO₂) just below normal or in the low-normal range, and normal bicarbonate (HCO₃⁻) levels.

Sion have no effect on saturation in patients with high-normal oxygen saturation. In our patient group, however, the mean is close to the descending part of the S curve, and a 1% decrease in saturation reflects a significant change in oxygen tension. In healthy individuals with normal cerebral circulation, a reduction in arterial oxygen tension is compensated for by cerebral vasodilatation; thus, mild hypoxia can be tolerated without changes in cerebral metabolism. Such compensation by
vasodilatation is not possible in the ischemic brain, rendering patients with stroke more sensitive to hypoxia.27,28

Results of the capillary blood gases suggest that most patients are hypocapnic and have a mild respiratory alkalosis. This may be due to central hyperventilation but may also reflect compensation of problems with gas exchange because arterial oxygen tension in this group was normal or low-normal rather than at the upper end of the range as expected with true hyperventilation.

Nocturnal hypoxia after the stroke may be due to preexisting comorbidity or to direct or indirect effects of the stroke on respiration and gas exchange. Because we do not have data on oxygen saturation before the stroke, it is not possible to say whether the difference in oxygen saturation between stroke patients and control subjects is due to the stroke rather than the higher prevalence of smokers, cardiovascular disorders, and sleep apnea in the stroke group. Nevertheless, the high prevalence of respiratory alkalosis may suggest an acute change in respiration and oxygenation over and above the effects of potential underlying chronic cardiovascular pathology.

In conclusion, hypoxia is a major problem early after a stroke. Fifty percent of stroke patients considered for this study had indications for oxygen treatment at recruitment. But even after they were excluded, many stroke patients who appear normoxic during the day may develop significant hypoxia at night early after the stroke. Regular monitoring of oxygen saturation throughout the day and night is therefore necessary to detect hypoxia reliably. The high prevalence of alkalosis with normal low oxygen tensions suggests that some normoxic patients may be able to maintain normal oxygen saturation only with increased respiratory effort and could benefit from oxygen supplementation.

Acknowledgments

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References

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