Effect of upper airway obstruction on blood pressure variability after stroke

Peter M. TURKINGTON*, John BAMFORD†, Peter WANKLYN‡ and Mark W. ELLIOTT* 

*Department of Respiratory Medicine, The Leeds Teaching Hospitals NHS Trust, St James’s University Hospital, Beckett Street, Leeds LS9 7TF, U.K., †Department of Neurology, The Leeds Teaching Hospitals NHS Trust, St James’s University Hospital, Beckett Street, Leeds LS9 7TF, U.K., and ‡Department of Elderly Medicine, The Leeds Teaching Hospitals NHS Trust, St James’s University Hospital, Beckett Street, Leeds LS9 7TF, U.K.

ABSTRACT

Approx. 60 % of acute stroke patients have periods of significant UAO (upper airway obstruction) and this is associated with a worse outcome. UAO is associated with repeated fluctuation in BP (blood pressure) and increased BP variability is also associated with a poor outcome in patients with acute stroke. UAO-induced changes in BP, at a time when regional cerebral perfusion is pressure-dependent in areas of critically ischaemic brain, could explain the detrimental effect of UAO on outcome in these patients. The aim of the present study was to examine the relationship between UAO and BP variability in patients with acute stroke. Twelve acute stroke patients and 12 age-, sex- and BMI (body mass index)-matched controls underwent a sleep study with non-invasive continuous monitoring of BP to assess the impact of UAO on BP control after stroke. Stroke patients had significantly more 15 mmHg dips in BP/h than the controls (51 compared with 6.7 respectively; \(P < 0.004\)). Stroke patients also demonstrated significantly higher BP variability than the controls (26.8 compared with 14.4 mmHg; \(P < 0.001\)). There were significantly more 15 mmHg dips in BP/h in stroke patients who had significant UAO than those who did not (85.7 compared with 29.5 respectively; \(P < 0.032\)). Furthermore, stroke patients without UAO (RDI < 10, where RDI is respiratory disturbance index) had significantly more 15 mmHg dips in BP/h than the controls (29.5 compared with 6.7 respectively; \(P < 0.037\)). There was a positive correlation between the severity of UAO (RDI) and 15 mmHg dips in BP/h (\(r = 0.574, P < 0.005\)) in stroke patients. Our results suggest that UAO alone does not explain BP variation post-stroke, but it does play an important role, particularly in determining the severity of the BP fluctuation.

INTRODUCTION

OSA (obstructive sleep apnoea) occurs in up to 71 % of stroke patients [1–5]. UAO (upper airway obstruction) has recently been shown [6,7] to be common in the first 24 h after onset of stroke, when the ischaemic brain is likely to be most vulnerable to secondary insults, with 61 % of patients demonstrating >10 apnoeas and hypopnoeas per hour.

BP (blood pressure) variability in patients with acute stroke has been shown [8,9] to be significantly higher than in age- and sex-matched controls during wakefulness and when breathing was controlled at a set rate. Dawson et al. [10] demonstrated that this BP variability is associated significantly with a poor outcome at 30 days.

Several haemodynamic oscillations are known to occur with obstruction of the upper airway in patients with OSA. In particular, BP decreases to a nadir at the
midpoint of the apnoea, due to the increasingly negative intrathoracic pressures generated by repeated respiratory efforts against an obstructed pharynx. BP will then rise gradually until apnoea termination when there will be an overshoot, thought to be due to resumption of respiration with arousal [11,12]. However, BP variability, defined as the S.D. of the beat-to-beat BP values [8,9], has not been demonstrated to be increased in patients with OSA.

UAO may contribute to, or cause, increased BP variability seen after stroke and, with the loss of cerebral autoregulation, cause further damage to the ischaemic penumbra. The aim of the present study was to examine whether there is an association between BP variability and UAO after stroke, both of which have been shown to be common.

METHODS

Subjects
Twelve patients, who had been admitted to the Leeds Teaching Hospital NHS Trust having suffered a CT-confirmed ischaemic stroke within the previous 24 h, were recruited. Stroke severity was assessed in each patient using the Scandinavian Stroke Scale [13]. Twelve controls, who were age-, sex- and BMI (body mass index)-matched to the stroke patients and gave no prior history of snoring, nocturnal apnoeas or choking, or daytime hypersomnolence, were recruited from patients admitted to hospital prior to routine minor surgery. None of the controls was prescribed sedatives on the night of their study. Control patients with a previous history of stroke or other chronic respiratory disorder (e.g. chronic obstructive pulmonary disease or asthma) were excluded. Written consent was obtained, and the study was approved by the Local Ethics Committee.

Sleep studies
Studies were carried out using the Alice 4 sleep system (Respironics, Paris, France). In the case of the stroke patients, these were started as soon as possible after admission and continued up to a total of 24 h or until patients requested that the equipment be removed (each patient had at least 6 h of data recorded during the night). Oronasal airflow (thermisistor), heart rate (ECG), oxygen saturation (finger probe), abdominal and respiratory effort (strain gauge), snoring (microphone), body position (sensor detecting eight points of compass on thoracic strain gauge) and light intensity (light meter) were recorded. All subjects were studied in their own hospital bed. Usual nursing and physiotherapy practices for the stroke patients were not altered during the study; in particular, the patient was positioned according to the usual ward practice. Ward staff 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 using standard criteria, with RDI (respiratory disturbance index) expressed per hour of study.

BP measurements
BP was recorded in each subject, for the entire duration of their sleep study, using Portapres (TNO Biomedical Instrumentation, Amsterdam, Holland). The unit has a height-correction device to compensate for any hydrostatic level effects due to movements of the hand. Portapres has been demonstrated previously [14–16] to provide an accurate estimate of invasive intra-arterial BP without disturbing sleep or causing discomfort [14]. The unit has two servo-controlled pressure cuffs which were placed around the middle and ring fingers. The non-hemiplegic arm was used in the stroke patients. The device records BP from each cuff, alternating every 30 min. Recorded continuous mean BP was analysed using the Beatscope software (TNO Biomedical Instrumentation) supplied with Portapres. A moving 10-s average BP was subsequently calculated, and each 10 and 15 mmHg dip below this value was recorded. BP variability was calculated using the S.D. of the beat-to-beat mean BP values. Comparisons were made in the number of dips in BP and BP variability.

Patterns of BP dips and association with UAO
To evaluate the effect of UAO alone on BP fluctuation, in terms of 10 and 15 mmHg dips, and to examine the patterns of BP dips, we added continuous BP recording overnight in 14 patients with suspected OSA being investigated in our sleep laboratory. These patients were separate to the main study population.

Definitions
Apnoea was defined as a cessation in airflow of 10 s or greater 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 two. Hypopnoea was defined as 50 % decrease in airflow associated with a 4 % oxygen desaturation. Cheyne–Stokes respiration was defined as central apnoea or hypopnoea alternating with hyperpnoea in a crescendo–decrescendo pattern. Significant UAO was defined as an RDI > 10. Episodes of central apnoea were included in the analysis, as it was felt that without an oesophageal pressure transducer it would have been difficult to accurately delineate obstructive and central events.
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 means and S.D. Data which did not approximate to a normal distribution are described as medians and IQR (interquartile range). Statistical difference between the groups was assessed using Student’s \( t \), \( \chi^2 \) or Mann–Whitney \( U \) tests where appropriate. Association between severity of UAO (RDI) and fluctuation in BP was determined by Pearson’s product correlation. A \( P \) value < 0.05 was considered to indicate statistical significance.

RESULTS
Subject demographics are shown in Table 1. Stroke patients were similar to the controls in terms of age, sex and BMI. The amount of sleep-disordered breathing in the two groups is also shown in Table 1; the majority of events were obstructive in nature (82 %) with only 11 % being central events and 7 % mixed apnoeas. An RDI > 10 was observed in 58 % of the stroke patients. The prevalence of hypertension (defined as systolic BP > 160 and/or diastolic BP > 90 mmHg prior to stroke or taking antihypertensive therapy) was not significantly different.

The median (IQR) Scandinavian Stroke Scale and Glasgow Coma Scale of the stroke group was 25 (13.5–44.5) and 15 (12–15) respectively, and half were unable to swallow safely. In all patients this was their first stroke. All diagnoses of stroke were subsequently confirmed by a CT scan of the brain within 72 h.

Table 2 shows the mean BP overnight and BP variability data. BP variability was significantly higher in stroke patients compared with the controls. The number of 10 and 15 mmHg dips in BP/h below a 10 beat moving average are also shown in Table 2. There were significantly more 10 and 15 mmHg dips in BP in the stroke patients compared with the controls.

The average length of each ‘dip’ in BP and the amount of time BP was more than 10 and 15 mmHg below the moving average is shown in Table 3. The length of each 10 and 15 mmHg dip in BP was not significantly different between the groups; however, the stroke patients spent significantly more time with a BP more than 10 and 15 mmHg dips in BP in the seven stroke patients with UAO (RDI > 10) than in the five without UAO (RDI < 10). However, stroke patients without UAO (RDI < 10) had significantly more 10 and 15 mmHg dips in BP than the control group (Table 4).

OSA patients who were studied separately had a mean (S.D.) age of 47.7 (12.3) years, 83 % were male and the mean (S.D.) BMI was 31.1 (5.6). Median (IQR) RDI was 13.4 (5.3–27.5) events/h. There was a median (IQR) 34 (25.4–62.1) and 13.9 (9.1–27.8) 10 and 15 mmHg dips/h respectively. This was statistically significantly less than that seen in our stroke patients with a comparable RDI (15 mmHg dips/h, 13.9 in OSA compared with 51 in
stroke groups; $P < 0.021$) and more than that seen in our control population (6.7; $P < 0.017$). The pattern of BP fluctuation appeared similar in the stroke patients in the present study compared with our group of OSA patients in that the majority of apnoeas were associated with an initial dip in BP followed by a rise at apnoea termination. However, there was a difference in the stroke patients response to snoring, which appeared to be more frequently associated with BP dips than in OSA patients. Furthermore, 28% of the BP dips in the stroke patients in the present study were not associated with any apnoea, hypopnoea or snoring. However, the prevalence of these non-respiratory event-related BP changes in the stroke patients appeared to be greater during periods when UAO was more severe.

**DISCUSSION**

The main objective of the present study was to investigate whether BP variability in the first 24 h after stroke is associated with UAO, both of which have been demonstrated to be common [1,3–5,8] and to affect prognosis adversely [2,10,17]. We found greater BP variability, expressed as the S.D. of the beat-to-beat BP recordings, in our stroke patients than in the control group. This was also greater than has been reported in other studies (26.8 compared with 15) [8,9]. However, in these studies, respiration was controlled at a set rate to minimize the effect of respiration on BP. In addition, patients were studied when awake rather than asleep. We found more 10 and 15 mmHg dips in BP occurring in acute stroke patients than in age-, sex- and BMI-matched controls. The acute stroke patients with UAO had almost three times more 10 and 15 mmHg dips in BP than those without UAO. There was a positive correlation between the number of dips in BP and the severity of UAO in the acute stroke patients.

However, as frequent BP fluctuation was seen in patients with stroke without UAO, our results suggest that UAO is not the only factor which increases BP variability in patients with acute stroke. Furthermore, as BP variability is likely to be greater when mean arterial BP is higher, at least some of the changes seen in the present study may have been due to the fact that mean BP was higher in the stroke patients.

Our data therefore suggest that UAO, which increases BP fluctuation, has a much greater effect in the acute stroke setting and appears to exacerbate the increased fluctuation in BP that occurs in patients with acute stroke. The mechanism by which obstructive apnoea causes fluctuation in BP has been documented previously [11,12]. If this occurs on a background of impaired baroreceptor control, secondary to acute stroke, even greater instability of BP control is possible.

We chose to study fluctuation in BP in terms of the fall from a moving baseline, because we hypothesized that any falls in BP could affect perfusion in critically ischaemic areas of the brain. Cerebral autoregulation is diminished after stroke [18], with regional cerebral perfusion becoming pressure-dependent. This is likely to have the greatest detrimental effect on the ischaemic penumbra within the first 24 h of onset of symptoms. It is not known whether it is the number of dips in BP or the time spent with ‘relative hypotension’ that will have the most effect; however, the results from the present study suggest that both are increased markedly in acute stroke patients with frequent UAO. We have demonstrated previously [6] that UAO is common in this crucial early period after stroke and that this is associated with a worse outcome at 6 months, both in terms of morbidity and mortality [19]. Exacerbation of BP instability in acute stroke by UAO, as suggested by the present study, may represent a pathophysiological link between UAO and adverse prognosis after stroke. Intervention studies are required to determine whether treatment of UAO with CPAP (continuous positive airways pressure) following stroke has any effect on BP variability and prognosis.

**REFERENCES**


© 2004 The Biochemical Society
Upper airway obstruction and blood pressure variability after stroke

9 Robinson, T. G., James, M., Youde, J. et al. (1997) Cardiac baroreceptor sensitivity is impaired after acute stroke. Stroke 28, 1671–1676