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# Acceptance, effectiveness and safety of continuous positive airway pressure in acute stroke: A pilot study

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## KEYWORDS

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Stroke;  
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Portapress;  
Cerebral blood flow velocity;  
Autoset

## Summary

**Objectives:** To evaluate the acceptance, effectiveness in preventing upper airways obstruction, and haemodynamic effects of continuous positive airway pressure (CPAP) in acute stroke.

**Methods:** Twelve patients (4 M, and 8 F; mean (SD), 75.2 (5.5) years) within 48 h of acute stroke onset underwent: (1) sleep studies (1st night: auto-CPAP mode; 2nd night: diagnostic); (2) nocturnal non-invasive blood pressure studies (1st night during CPAP; 2nd night during spontaneous breathing (SB)); and (3) daytime cerebral blood flow velocity measurement in middle cerebral artery (FV) with transcranial Doppler during SB and with CPAP (5, 10, 15 cmH<sub>2</sub>O).

**Results:** Ninety percent, 60% and 50% of stroke patients had a respiratory disturbance index (RDI) of  $\geq 5$ ,  $\geq 10$  and  $\geq 15$  events per hour, respectively (18.2 (11.3)). CPAP acceptance was 84%; 42% used CPAP more than 6 h and 42% between 1–3 h with a mean use of CPAP of 5.2 h (4.0). Compared to SB, CPAP reduced, though not significantly, RDI, time with SaO<sub>2</sub> < 90%, mean blood pressure and mean blood pressure dips (10 mmHg)/h. Compared with SB, any level of CPAP progressively and significantly reduced systolic and mean FV; drop in diastolic FV was significant at CPAP10 and CPAP15. The partial pressure of end-tidal CO<sub>2</sub> was significantly lowered by all levels of CPAP.

**Conclusions:** According to this pilot study, CPAP is reasonably well tolerated by patients with acute stroke for at least one night. Despite its possible beneficial effect on obstructive sleep-disordered breathing and blood pressure variability, CPAP use in acute stroke should be still considered with caution due to possible harmful haemodynamic effects at higher pressures.

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## Introduction

There is an emerging evidence base of an association between sleep-disordered breathing (SDB) and cerebrovascular disease, suggesting that obstructive sleep apnoea (OSA) is an independent risk factor for stroke proportional to severity.<sup>1–7</sup> The relationship between OSA and stroke is further supported by several studies which found a significant prevalence of SDB (especially OSA) (43–95%) in patients with recent cerebrovascular accidents.<sup>7–16</sup> It is not clear whether SDB may be regarded as a consequence of, or as a cause of stroke, or both. Regardless of whether SDB precedes or follows a stroke, some data suggested that it may adversely affect both the functional outcome at 3 and 12 months<sup>8</sup> and the mortality at 6 months, 2 and 4 years<sup>7,17,18</sup> of patients with acute stroke. Moreover, recent studies demonstrated that sleep-related stroke and the early neurological worsening of stroke were independently predicted by the degree of respiratory disturbance index (RDI) and by the presence of SDB, respectively.<sup>13,16</sup>

Only two studies<sup>12,13</sup> showed a high prevalence of SDB, mostly due to obstructive events, within the first 24 h of stroke, when the critical phenomenon of the ischaemic penumbra is taking place.<sup>19</sup> In the acute phase of stroke the physiological consequences of recurrent obstructive apnoeas may have the most deleterious effect on critically ischaemic, but viable, brain tissue and, therefore, may adversely affect prognosis. Systemic and cerebral haemodynamic fluctuations and/or episodes of hypoxia are known to accompany occlusion of the upper airway in patients without stroke. Specifically, systemic blood pressure (BP), pulse rate and cardiac output all decrease during an obstructive apnoea and increase suddenly when arousal ends the apnoea.<sup>20</sup> Moreover, cerebral blood flow velocity decreases during upper airway obstruction<sup>21</sup> and cerebrovascular reactivity is impaired in OSA patients.<sup>22</sup>

We postulated that application of continuous positive airway pressure (CPAP) would be the treatment of choice for OSA<sup>23</sup> in the first hours after stroke. CPAP may reduce morbidity and mortality by preventing episodes of upper airway obstruction and their haemodynamic and hypoxic effects upon ischaemic cerebral tissue. To confirm this hypothesis, a prospective interventional trial is needed. However, CPAP in the acute phase of stroke could have harmful effects. Firstly, application of CPAP in patients with acute stroke may be problematic for several reasons (i.e., age, cognitive and communication deficits, facial palsy). Secondly, BP may be reduced by CPAP in patients in whom cardiac output is likely to be preload-dependent and who may be dehydrated.<sup>24</sup> Thirdly, as in healthy subjects,<sup>25</sup> cerebral blood flow velocity may drop with CPAP due to hypocapnia-induced cerebral vasoconstriction.

This pilot study aims to establish: (1) the feasibility of delivering CPAP to patients in the acute phase of stroke; (2) the effectiveness of CPAP in preventing obstructive events and its associated cardiovascular fluctuations; and (3) the safety of CPAP in terms of systemic and cerebrovascular haemodynamics.

## Methods

### Patients and study design

We prospectively studied 12 consecutive patients with a clinical and CT-based diagnosis of acute stroke admitted to the Stroke Unit of the Leeds General Infirmary. Inclusion criteria were: symptom onset < 48 h; body mass index > 22 Kg/m<sup>2</sup>; and neck circumference > 34 cm (female) and > 37 cm (male). The study was carried out in accordance with the Declaration of Helsinki (2000) of the World Medical Association and was approved by the Ethics Committee of the Hospital; informed, written consent was obtained from all patients or, if they were unable, their next of kin. Consent was sought as soon as possible after admission and the studies were started directly thereafter. Exclusion criteria were: vomiting since stroke; uncontrolled agitation or confusion; and refusal of consent.

The design of the study consisted of (1) titration and diagnostic sleep studies; (2) non-invasive BP overnight studies (1st night during CPAP; 2nd night during spontaneous breathing (SB)); and (3) daytime cerebral blood flow velocity measurement in the middle cerebral artery (FV) with transcranial Doppler (TD) during SB and at increasing levels of CPAP.

### Patient assessment

On admission all patients underwent a comprehensive assessment that included: age, sex, body mass index, neck circumference, history of snoring, previous cerebrovascular accidents, hypertension, diabetes mellitus. Daytime sleepiness preceding stroke was estimated by the Epworth Sleepiness Scale (ESS).<sup>26</sup> Pre-stroke disability and handicap were assessed with the Barthel Index<sup>27</sup> and the modified Rankin Scale, respectively.<sup>28</sup>

Diagnosis and location of stroke was confirmed by means of a CT brain scan performed within 72 h of admission to the Stroke Unit. Stroke subtypes were clinically classified according to the Oxford Community Stroke Project<sup>29</sup>: total anterior circulation syndrome (TACS), partial anterior circulation syndrome (PACS), lacunar syndrome (LACS), and posterior circulation syndrome (POCS). Stroke severity was assessed using the Scandinavian Stroke Scale.<sup>30</sup> Level of consciousness (Glasgow Coma Scale),<sup>31</sup> limb weakness (Motricity Index)<sup>32</sup> and the modified Rankin Scale<sup>28</sup> were documented on admission.

### Titration and diagnostic sleep studies

Sleep studies were performed with the Autoset Portable II Plus (ResMed, Sydney, Australia), which allows both diagnostic and CPAP titration of patients with SDB.<sup>33</sup> Several investigations reported a similar accuracy of a portable, automatic CPAP device compared to conventional polysomnography.<sup>34–36</sup> Furthermore, Bassetti et al<sup>16</sup> found a good correlation ( $r^2 = 0.75$ ) between the apnoea–hypopnoea index as estimated by polysomnography and automatic CPAP device in 31 acute stroke patients.

As soon as possible, after recruitment to the study, an explanation of CPAP was given to the patients; they then

underwent a short acclimatisation trial with the aim of choosing an interface (nasal or facial mask; Sullivan; Mirage ResMed) and establishing the maximum pressure which could be tolerated without significant leak. During the first night patients received CPAP in automatic mode<sup>33</sup> with lower and upper pressure limits of 4 and 10 cmH<sub>2</sub>O, respectively; this was switched to manual mode if the automatic mode was not tolerated. Oxygen saturation and heart rate (finger pulse oximeter probe), snoring, airflow and flow limitation (pressure transducer), body position and respiratory effort (strain gauge) were recorded. Usual nursing care, patient positioning included, was not changed during the study. Nursing staffs were instructed to check CPAP acceptance throughout the night. To avoid increasing distress to the patients in this critical phase after stroke, CPAP was taken off when any signs of discomfort became evident. CPAP acceptance rate was expressed according to the number of hours tolerated, as "higher" (H) or "lower" (L) than 3 h. Refusal of CPAP occurred if patients did not tolerate the machine for more than 1 h.

The second night following recruitment, the patients underwent a diagnostic study (mean (SD) length, 6.2 h (2.5)) during SB with the same device but with nasal cannulae positioned to measure nasal airflow instead of the CPAP mask.

Each study was individually performed and scored by the same physician (RS). RDI was subsequently calculated as the number of apnoeas and hypopnoeas per hour of study. An apnoea was scored if the 2-s moving average ventilation dropped below 25% of the recent average (time constant 100 s) for  $\geq 10$  s. An hypopnoea was defined as a 50–75% decrease in ventilation for  $\geq 10$  s. The analysis was limited to obstructive events since the identification of central events is not reliable with this diagnostic portable device.<sup>33</sup> The severity of SDB was classified depending on the level of RDI  $\geq 5$ ,  $\geq 10$  and  $\geq 15$  events per hour. Index of 4% oxygen desaturation and percentage of time with SpO<sub>2</sub> < 90% were also recorded.

### Non-invasive haemodynamic nocturnal studies

Beat to beat non-invasive BP was monitored with the Portapres model 2 device (TNO-TPD, Biomedical Instrumentation)<sup>37</sup> during CPAP (first night) and during SB (second night). The Portapres device is based on the arterial volume clamp method of Pénáz and measures BP through two small finger cuffs wrapped around the middle and ring fingers of the hand of the dominant arm, which are alternately used every 30 min to avoid the discomfort associated with prolonged measurements from one finger only. The device also includes a system capable of automatically correcting for changes in finger pressure induced by changes in the level between the heart and the instrumented finger, due to hand displacement. All data were analysed off-line; analog signals were A/D converted with a 0.25 mmHg resolution at 100 Hz real time and analysed by dedicated software (BeatScope, TNO-TPD, Biomedical Instrumentation). Systolic, diastolic, mean BP, as well as pulse interval and its inverse, pulse rate, were derived from each single pulse wave by the Beatfast program. All data were averaged by time in seconds; the recorded segments containing the automatic calibration signal and artefacts were removed from the Portapres traces.

To investigate BP variability we calculated the number of mean BP dips  $\geq 10$  mmHg/h as the mean difference between the mean BP value of a single pulse and the average of mean BP of the previous 10 pulses.

### Cerebral blood flow velocity measurements in the middle cerebral artery

Systolic, diastolic and mean FV were assessed by using a 2 MHz-pulsed TCD device (SciMed PC Dop 842AQ; SciMed, Bristol, UK). After the diagnostic sleep study, each subject was investigated during the day while awake and supine during SB and CPAP, via a nasal or a facial mask. Using a previously described protocol,<sup>25</sup> all subjects were examined for 3 min in each of the following stages: before (SB) and with increasing levels of CPAP (Sullivan ResMed® UK Ltd.) at 5, 10 and 15 cmH<sub>2</sub>O (CPAP5, CPAP10, CPAP15) taking care to avoid air leaks.

The probe, fixed with an elastic headband, was placed over the temporal bone, just above the zygomatic arch in order to obtain a continuous measurement of FV. The M1 segment of the middle cerebral artery was sought at a depth of approximately 50 mm, keeping the insonation angle constant throughout the investigation.<sup>38</sup> Measurement was performed on one or both sides depending on patient tolerance. The test was interrupted if the patient showed any signs of discomfort. Partial pressure of end-tidal CO<sub>2</sub> (PetCO<sub>2</sub>) was recorded continuously with an infrared analyser (Morgan Capnograph, PK Morgan Ltd., Rainham, Kent, UK). In order to minimise the potential error of dilution on PetCO<sub>2</sub> measurement due to the CPAP bias flow, a thin catheter was inserted through a T-tube situated between the mask and the expiratory port; the end of the catheter was positioned just into one nostril. Particular attention was paid to obtain a reliable capnographic trace throughout the tests.<sup>25</sup>

### Statistical analysis

All data are expressed as mean (SD) except for ordinal data derived from various scales which are described as median (interquartile range (IQR)). Statistical comparisons were made with two-tailed Student's *t*-test or Mann–Whitney or Chi-square test where appropriate. For multiple comparison of FV and PetCO<sub>2</sub> at the different stages of TCD study the repeated measures ANOVA test was applied. SB values were compared with CPAP5, CPAP10, CPAP15 values by means of post hoc analysis (Bonferroni test) if the ANOVA test was significant. Correlation between percentage changes of FV and PetCO<sub>2</sub> were tested with linear regression by applying the least-squares method.

A value of  $p < 0.05$  was assumed to be statistically significant. Analyses were performed using version 10.0 of the SPSS statistical software package for Windows (SPSS, Inc., Chicago, Illinois).

### Results

All patients enrolled in the study had a diagnosis of ischaemic stroke confirmed clinically and radiologically. Demographic and pre-stroke clinical characteristics of the

population studied are shown in Table 1. Some of the recruited patients could not fill in the ESS questionnaire independently, but all of them were able to read and/or understand the items of the ESS and to answer the questions with support. Although it has not been validated for use in this way it was not an end point in this study, but rather was used to help define the study population.<sup>26</sup> Delay from estimated time of onset of first stroke symptom and start of the CPAP sleep study was 21.8 h (15.5). Admission to the emergency department occurred 3.3 h (3.8) after symptom onset. Stroke features are described in Table 2. Fig. 1 shows the study protocol.

### Titration and diagnostic sleep studies

Acceptance of CPAP was reported in 84% of cases (10/12) with a mean use of CPAP of 5.2 h (4.0) (range 1.5–11). Refusal of CPAP in two cases was due to claustrophobia and agitation within 30 min of CPAP application. Causes of CPAP withdrawal in L group were: late onset mask discomfort (3 cases), excessive air pressure (1 case), and mask dislodgement (1 case). A nasal mask was used in 6 cases; in two cases CPAP was switched from automatic to manual mode. The median pressure in the 10 patients who accepted CPAP was 6 cmH<sub>2</sub>O (1.7) (95th percentile, 8 cmH<sub>2</sub>O (1.6)); the pressure waves in the downloaded graphs did not show long periods of plateau at upper pressure limit as if central events were the most prevalent sleep pattern. Compared to L group, patients of H group showed a trend towards a greater sleepiness score (12 (5–12.5) versus 7 (5–12.5)), worse stroke severity (38 (11–46) versus 24 (18–41)) and greater limb weakness (122 (0–182) versus 74 (0–136)).

The diagnostic sleep study was performed 48.2 h (16) after the estimated onset of stroke symptoms in all but two cases: one with a high acceptance of CPAP in the first night had a sudden respiratory arrest the following day due to a further brainstem stroke; another patient, who did not tolerate CPAP, refused to continue the study. Ninety percent, 60% and 50% of stroke patients had an RDI of  $\geq 5$ ,

$\geq 10$  and  $\geq 15$  events per hour, respectively (mean (SD), 18.2 (11.3)). CPAP acceptance in patients with higher degrees of SDB (RDI  $\geq 10$ ) was 83.3% (5/6 patients) with a mean use of 3.7 h (4.1).

Table 3 shows the sleep studies data. In 9 patients compliant to CPAP (L and H groups), there was a non-significant trend to a reduced RDI (17.7 (12.5) versus 11.3 (8.8)) and time with SaO<sub>2</sub> < 90% (8.1 (14.7) versus 0.6 (0.9)) in the SB versus CPAP assessments.

### Non-invasive BP nocturnal studies

Haemodynamic monitoring was performed both during CPAP and SB nights in 8 of 10 patients adherent to CPAP. A trend towards a drop in mean BP and in BP variability was observed during CPAP (Table 4).

### Cerebral blood flow velocity measurements in the middle cerebral artery

Fourteen measurements of FV were obtained in 9 patients all with RDI  $\geq 5$  event per hour (7 were recorded from the affected cerebral side); in 5 subjects the study was performed on both sides. Measurements were made 53.1 h (23.4) after the estimated time of stroke symptoms onset, once the second sleep study was ended. In most cases (11/14) a facial mask was used. EtCO<sub>2</sub> trace was reliable in 8 cases.

Compared to SB, any level of CPAP progressively and significantly reduced systolic and mean FV; the drop in diastolic FV was significant at CPAP10 and CPAP15. PetCO<sub>2</sub> was significantly lowered by all levels of CPAP (Table 5). The fall in systolic FV was significantly correlated with the reduction in PetCO<sub>2</sub> at CPAP10 ( $r = 0.861$ ;  $p = 0.006$ ).

### Discussion

This pilot study was conducted within the first 48 h of acute stroke in 12 patients with the aims of clarifying whether CPAP is feasible, effective in preventing obstructive events and its associated cardiovascular

**Table 1** Demographic and pre-stroke clinical characteristics.

Variable	Value
Age, yrs	75.2 (5.5)
Sex, <i>n</i> (%) male	4 (33.3)
Body mass index, kg/m <sup>2</sup>	26.6 (4.7)
Neck circumference, cm	41.2 (4.5)
Epworth Sleepiness Scale, median (IQR)	10.5 (6.3–13)
History of snoring, <i>n</i> (%)	9 (75)
Hypertension, <i>n</i> (%)	6 (50)
Diabetes mellitus, <i>n</i> (%)	1 (8.3)
Modified Rankin score, median (IQR)	2 (1.25–2)
Barthel Index, median (IQR)	16.5 (14–18.8)

All data are expressed as mean (standard deviation) unless differently stated.  
IQR: interquartile range.

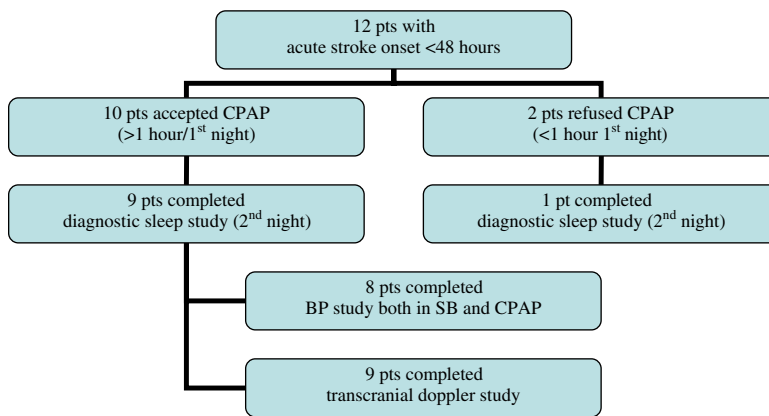
**Table 2** Stroke characteristics.

Variable	Value
First stroke, <i>n</i> (%)	6 (50)
Scandinavian Stroke Scale	31 (17–42)
Motricity index	97 (0–151.8)
Modified Rankin score	5 (4–5)
Glasgow Coma Scale	15 (13–15)
TACS, <i>n</i> (%)	5 (41.7)
PACS, <i>n</i> (%)	3 (25)
POCS, <i>n</i> (%)	0 (0)
LACS, <i>n</i> (%)	4 (33.3)

All data are expressed as median (interquartile range) unless differently stated.

TACS: total anterior circulation syndrome; PACS: partial anterior circulation syndrome; POCS: posterior circulation syndrome; and LACS: lacunar syndrome.





**Figure 1** Flow chart of the study protocol. CPAP = continuous positive airway pressure; SB = spontaneous breathing; BP = blood pressure.

fluctuations, and safe in terms of systemic and cerebrovascular haemodynamics. It was confirmed that SDB was common in the acute phase of stroke, with 60% of patients having RDI of  $\geq 10$  events per hour. The acceptance rate of CPAP was variable with 42% of patients using the machine for  $>6$  h and 42% for 1–6 h. In the patients who used CPAP, there was a trend to a reduced RDI and length of time with  $\text{SaO}_2$  below 90%. Non-invasive systemic haemodynamic monitoring showed a non-significant reduction in both mean BP and BP fluctuations during CPAP compared to SB. FV measured during the day was significantly impaired by increasing levels of CPAP given for a short trial, which also caused significant hypocapnia.

The prevalence of SDB found in our study was similar to that reported by other authors in acute stroke ( $<5$  days since symptom onset).<sup>12–14</sup> As our study protocol involved additional equipment for the haemodynamic investigation, we performed the diagnostic sleep study with a limited, less complicated but validated system (Autoset Portable II Plus)<sup>16,34–36</sup> because more intrusive full polysomnography would have not been tolerated by agitated and dependent stroke patients.<sup>11</sup> However, sleep duration, stage and quality cannot be assessed with this kind of respiratory variable-only monitoring systems. Moreover, central sleep apnoea and/or Cheyne–Stokes respiration (CSA/CSR), which may occur in acute stroke,<sup>9</sup> could not be detected with the Autoset diagnostic system. However, studies of SDB in acute stroke show that most events are obstructive

with central events being uncommon<sup>7,8,10,12,14</sup> except in patients with coexistent left ventricular dysfunction.<sup>39</sup> Because the denominator for the calculation of RDI is total study time rather than total sleep time, the Autoset tends to underestimate the severity of SDB.

Our finding of 42% of all patients included into the study with high acceptance of CPAP with the Autoset system is similar to the results of the previous investigations performed in the earlier phase of the stroke (47–69%)<sup>14,16</sup> and, not surprisingly, lower than those reported in the rehabilitation post-stroke setting in selected and much younger patients (70.5–100%).<sup>15,40,41</sup> This study reports the first patients treated with CPAP in our unit and inevitably there was a learning curve. It is probable that with increasing familiarity, particularly of the nursing staff, acceptance and compliance would increase.

Interestingly, in our study, patients with better tolerance of CPAP showed a trend towards a greater sleepiness score, worst stroke severity and greater limb weakness. Likelihood of pre-stroke OSA (i.e., greater sleepiness score) and severe motor defect may improve the acceptance of CPAP in acute stroke. Statistical analysis did not reach significance for these variables probably due to the small size of the sample.

The lack of a significant effect of CPAP on SDB may be at least in part due to the occurrence of CSA/CSR in our patients as well as to the small size of the sample. It has been shown that “pure” CSA/CSR events may be more effectively managed by the use of adaptive servo-ventilation

**Table 3** Sleep studies data.

	SB	CPAP	<i>p</i> -value
Time with $\text{SaO}_2 < 90\%$ , %	16.7 (29.2)	0.6 (0.9)	$>0.05$
Oxygen 4% desaturation index, <i>n</i> /h	18.1 (9.4)	9.7 (10.7)	$>0.05$
RDI, <i>n</i> /h	18.2 (21.3)	10.9 (8.4)	$>0.05$
RDI $> 10$ , <i>n</i> (%)	6 (60)	4 (40)	$>0.05$

All data are expressed as mean (standard deviation), unless differently stated.

SB: spontaneous breathing; CPAP: continuous airway pressure; and RDI: respiratory disturbance index.

**Table 4** Haemodynamic nocturnal data.

	SB	CPAP	<i>p</i> -value
Systolic BP, mmHg	155.8 (17.1)	140.8 (34.9)	$>0.05$
Diastolic BP, mmHg	69.9 (11.8)	70.1 (20.8)	$>0.05$
Mean BP, mmHg	98.6 (7.2)	94.2 (22.6)	$>0.05$
Mean BP dips $\geq 10$ mmHg $\text{h}^{-1}$ , <i>n</i>	299 (227)	219 (110)	$>0.05$

All data are expressed as mean (standard deviation).

SB: spontaneous breathing; CPAP: continuous airway pressure; and BP: blood pressure.

**Table 5** Transcranial Doppler data.

	SB	CPAP5	CPAP10	CPAP15	Significance <sup>a</sup>
Systolic FV cm s <sup>-1</sup>	66.9 (27.6)	60.4 (28.3) <sup>b</sup>	58.4 (28.1) <sup>b</sup>	50.6 (22.4) <sup>b</sup>	<i>p</i> = 0.001
Diastolic FV cm s <sup>-1</sup>	20.3 (12.3)	19.0 (11.7)	18.6 (11.1) <sup>b</sup>	16.8 (8.5) <sup>b</sup>	<i>p</i> = 0.045
Mean FV cm s <sup>-1</sup>	36.5 (18.0)	33.6 (18.5) <sup>b</sup>	32.5 (17.2) <sup>b</sup>	28.7 (13.5) <sup>b</sup>	<i>p</i> = 0.007
PetCO <sub>2</sub> Kpa	5.6 (1.5)	5.0 (1.3) <sup>b</sup>	4.7 (1.2) <sup>b</sup>	4.4 (1.2) <sup>b</sup>	<i>p</i> < 0.0001

All data are expressed as mean (standard deviation).

SB: spontaneous breathing; CPAP: continuous airway pressure; FV: cerebral blood flow velocity; and PetCO<sub>2</sub>: and end-tidal CO<sub>2</sub> partial pressure.

<sup>a</sup> Represents significance as measured by repeated measures ANOVA test.

<sup>b</sup> Represents significant changes from baseline value as measured by post hoc analysis.

than either CPAP or oxygen therapy in terms of improvement in breathing pattern, sleep quality and stability of PaCO<sub>2</sub> level.<sup>42</sup>

All patients had CPAP followed by a diagnostic study and, while this might seem illogical, if CPAP is to have an effect on the ischaemic penumbra, it must be started as soon as possible. For the purposes of this pilot study it was important to understand whether these patient did indeed have upper airway obstruction and to understand the effect of CPAP on SDB and haemodynamics. In future randomized controlled trials, patients would either have CPAP or a diagnostic study on the first night. Secondly, we performed the CPAP titration before the sleep diagnostic study in order to avoid an over-estimation of CPAP effects on SDB. Stroke patients might show spontaneous improvement between study nights as any acute cerebral oedema resolves.<sup>9</sup>

A trend of reduction in overnight mean BP, and in its variability, was observed with CPAP in acceptant patients. Effective CPAP which prevents obstructive events and their physiological consequences, such as hypoxemia and cardiovascular fluctuations, may reduce the damage to the ischaemic, but viable, penumbra in the crucial first hours of acute stroke.<sup>19</sup> On the other hand, the finding of a trend towards a drop in BP with CPAP could have harmful effects upon cerebral perfusion in ischaemic tissue. In fact, as autoregulation may be locally impaired in acute stroke,<sup>43</sup> cerebral perfusion may become "pressure-dependent". Moreover, FV as measured with TCD was reduced by increasing levels of CPAP; FV allow a good estimation of cerebral blood flow as it is widely accepted that changes in cerebral perfusion through the large arteries on the surface of the brain, such as the middle cerebral artery, are mainly due to changes of velocity, with only insignificant changes of vessel diameter.<sup>38</sup> In acute stroke, these cerebrovascular changes with CPAP could enhance the negative effects of falls in systemic blood pressure upon ischaemic cerebral tissue. As we found in normal subjects,<sup>25</sup> the CPAP-induced FV drop was associated with a reduction in PetCO<sub>2</sub> in stroke patients; so the effect of CPAP upon FV might be at least partially due to the constriction of small cerebral resistance vessels because of hypocapnia.

Some important issues have been raised by this study. The potential for CPAP, certainly at higher levels, to result in undesirable physiological changes, is confirmed, though it is not known whether the fall in BP and FV seen in the daytime study are clinically relevant. The interpretation of the effects on FV should be made with caution as they were obtained after a short trial of CPAP. Patients breathing with

a mask when it is first put on may hyperventilate, though of note by the time the transcranial Doppler study was performed they had used CPAP overnight, lowering carbon dioxide and affecting FV. This hyperventilation may not be sustained with longer use or during sleep overnight. The effects were not surprisingly more marked at higher CPAP pressures, although any potential harmful effects may be offset by the beneficial effects of abolishing obstructive SDB and its haemodynamic sequelae and hypoxia. It would seem reasonable in any future studies to cap CPAP pressure at 10 cmH<sub>2</sub>O, as pressures above this level may have harmful haemodynamic effects and do not seem to be necessary anyway to control the sleep-disordered breathing (mean CPAP pressure of 6 cmH<sub>2</sub>O in the sleep study).

Even though oxygen therapy may have a role in correcting, at least partially, hypoxemia induced by CSA/CSR, it has no effects on severe obstructive events and would have no effect on the blood pressure fluctuations.<sup>42</sup> Preventing hypocapnia by the addition of CO<sub>2</sub> to the circuit prevents the CPAP-induced fall in FV in normal subjects<sup>25</sup> and this could be achieved by repositioning of the exhaust port in the CPAP circuit to increase the dead space and, therefore, rebreathing. Any CPAP-induced fall in BP might be prevented by ensuring adequate hydration and avoidance of hypotensive agents.

Our data suggest that CPAP is reasonably well tolerated by patients with acute stroke for at least one night, but do raise some concerns about possible harmful effects at higher pressures. Larger scale studies should now be undertaken to test the hypothesis that CPAP can reduce secondary damage to the ischaemic penumbra due to obstructive SDB-induced cardiovascular variability and hypoxia.

### Conflict of interest statement

The authors have reported no conflicts of interest.

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