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Treatment of obstructive sleep apnoea with nasal continuous positive airway pressure in stroke

T.E. Wessendorf*, Y-M. Wang#, A.F. Thilmann#, U. Sorgenfrei#, N. Konietzko*, H. Teschler*

Treatment of obstructive sleep apnoea with nasal continuous positive airway pressure in stroke. T.E. Wessendorf, Y-M. Wang, A.F. Thilmann, U. Sorgenfrei, N. Konietzko, H. Teschler. ©ERS Journals Ltd 2001.

ABSTRACT: The prevalence of obstructive sleep apnoea (OSA) following stroke is high and OSA is associated with increased morbidity, mortality and poor functional outcome. Nasal continuous positive airway pressure (nCPAP) is the treatment of choice for OSA, but its effects in stroke patients are unknown.

The effectiveness and acceptance of treatment with nCPAP in 105 stroke patients with OSA, admitted to rehabilitation was prospectively investigated. Subjective wellbeing was measured with a visual analogue scale in 41 patients and 24-h blood pressure was determined in 16 patients before and after 10 days of treatment. Differences were compared between patients who did and did not accept treatment.

There was an 80% reduction of respiratory events with concomitant increase in oxygen saturation and improvement in sleep architecture. No serious side-effects were noticed. Seventy-four patients (70.5%) continued treatment at home. Nonacceptance was associated with a lower functional status, as measured by the Barthel Index, and the presence of aphasia. Ten days after initiation of nCPAP, compliant users showed a clear improvement in wellbeing (differences in visual analogue scale (ΔVAS) mean±SD 26±26 mm) *versus* noncompliant patients (ΔVAS 2±25 mm, p=0.021). Only the compliant group had a reduction in mean nocturnal blood pressure (ΔBP; -8± 7.3 mmHg *versus* 0.8±8.4 mmHg, p=0.037).

Stroke patients with obstructive sleep apnoea can be treated effectively with nasal continuous positive airway pressure and show a similar improvement and primary acceptance to obstructive sleep apnoea patients without stroke. Continuous positive airway pressure acceptance is associated with improved wellbeing and decreased nocturnal blood pressure.

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*Dept of Respiratory and Sleep Medicine, Ruhrlandklinik, and #Dept of Neurology, Fachklinik Rhein/Ruhr, Essen, Germany.

Correspondence: T.E. Wessendorf, Ruhrlandklinik, Dept of Respiratory and Sleep Medicine, Tueschener Weg 40, D 45239 Essen, Germany.
Fax: 49 2014334049

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The prevalence of sleep-disordered breathing (SDB) among patients with stroke is high [1–3]. The commonest pattern of SDB is obstructive sleep apnoea (OSA). Although stroke can cause central sleep apnoea, most patients have OSA preceding the cerebrovascular event [4]. OSA is a risk factor for hypertension and possibly for stroke. Therefore, treatment of OSA in patients with stroke might be considered as secondary prevention.

Nasal continuous positive airway pressure (nCPAP) is a highly effective treatment for OSA [5] and is widely regarded as the treatment of choice [6]. However, anecdotal experience suggests that continuous positive airway pressure (CPAP) is not well tolerated by stroke patients [7]. Given its high effectiveness even in mild OSA [8], it seemed logical to determine its role in patients with stroke. As Good *et al.* [7] showed that SDB in stroke may be associated with a worse outcome [7], CPAP might improve daily functional status and long-term morbidity. Apnoea and hypopnoea in association with sympathetic activation cause temporary increases in blood pressure [9], can lead to elevated blood pressure during the daytime and ultimately, sustained hypertension [10, 11]. Since abolition of OSA by CPAP might reduce blood pressure fluctuations and hypertension its use could be an important part of stroke management in those patients with OSA.

However, the potential problems with CPAP treatment in this population are numerous: the patients are generally older and due to their functional disability, may be unable to handle the mask and device. Cognitive deficits may hinder understanding of the importance of CPAP treatment, known to be of crucial importance for high acceptance and compliance. Soon after stroke, a high proportion of central apnoeas might limit the usefulness of CPAP. In addition, the presence of a facial palsy may contribute to significant mouth leak, known to cause nasal and pharyngeal mucosal problems, worsening of sleep quality and poorer compliance [12, 13]. Finally, the relatively low subjective sleepiness observed in stroke victims may interfere with patient acceptance, since CPAP use is in general, greater among sleepy patients [14].

The aim of the present study was, therefore, to

Table 1. – Baseline characteristics of the study population

Sex	
Female	25 (23.8)
Male	80 (76.2)
Age yrs	60.9 (59.2–62.8)
BMI $kg \cdot m^2$	28.7 (27.7–29.7)
Epworth score	7.2 (6.1–8.2)
$RDI \cdot h^{-1}$	37.9 (33.9–42.0)
Minimal S_{a,O_2} %	75.0 (73.9–77.6)
Barthel index	77 (71.3–82.0)
Aphasia	
Aphasia present	14 (13.3)
No aphasia	91 (86.7)
Days after stroke*	60 (50.6–69.3)

Data are presented as n (%) or mean (95% confidence interval). BMI: body mass index; RDI: respiratory disturbance index; S_{a,O_2}: arterial oxygen saturation. *: 17 patients had evidence of more than one cerebrovascular event. For those patients, the last event leading to rehabilitation was used.

prospectively investigate the effectiveness, acceptance, and effects on subjective wellbeing and blood pressure of nCPAP treatment in stroke patients with OSA.

Methods

The diagnosis of stroke was confirmed by two experienced neurologists and based on the referral diagnosis, a complete neurological history and examination, and reported computed tomography (CT) or magnetic resonance imaging (MRI) findings. Functional disability at the time of admission was assessed by the Barthel index. The presence of aphasia (defined as any sign of aphasia with no further differentiation) was determined.

Subjects with confirmed stroke were first screened for likely OSA on the basis of a history of snoring and positive cardiorespiratory screening using the Edentec II Plus device (Mallinckrodt, St. Louis, MO, USA) on the ward. The diagnosis of OSA was confirmed by overnight polysomnography (Compumedics, Melbourne, Australia) in 105 stroke patients (75 males, 30 females). Prior to polysomnography, the subjective level of sleepiness was evaluated using the Epworth sleepiness scale. The patient characteristics are given in tables 1 and 2.

Polysomnography was performed between 22:00–07:00 h. Two-channel electroencephalogram (EEG), electrooculogram (EOG) and chin electromyogram (EMG) were recorded using standard methods, as described [3]. Sleep data were staged manually according to standard criteria [15] and arousals were scored according to American Sleep Disorders Association (ASDA) criteria [16]. An apnoea was defined as cessation of airflow or reduction of the thermistor signal to <10% of baseline with a duration of $\leqslant$10 s. Apnoeas shorter than 10 s were counted if they were followed by either an arousal or an oxygen desaturation of $\geqslant$4%. Differentiation was made between obstructive (including mixed with a clear obstructive component) and central apnoeas according to the respiratory effort channels (absence of ribcage and abdominal movement). Hypopnoea was defined as a discernible reduction in the thermistor signal for $\leqslant$10 s followed by either an arousal or a desaturation of $\geqslant$4%. The respiratory disturbance index (RDI) was calculated as the number of all respiratory events per hour sleep.

Table 2. – Stroke characteristics

Localization	Patients n	Side of lesion*		Type of stroke	
		Right	Left	Ischaemic	Haemorrhagic
Hemispheric	90	51	39	74	16
Brainstem	13	7	6	13	0
Cerebellar	2	1	1	1	1
Total	105	59	46	88	17

*: 17 patients had evidence of more than one cerebrovascular event. For those patients, the last event leading to rehabilitation was used.

Criteria for initiation of treatment

Patients with obstructive or predominantly obstructive SDB and an RDI $\geqslant$15 were eligible for CPAP titration. The therapy and any possible side-effects were explained to patients. The current opinion about the impact of treatment was explained, *i.e.* that stroke patients could benefit from normalized breathing at night. Patients had to be able to remove the masks. Masks were fitted in the afternoon before the titration night, but no training session prior to titration was offered.

Titration

CPAP titration was performed under full polysomnographical control in the sleep laboratory with the AutoSet® (ResMed, Sydney, Australia), as described elsewhere [17]. In four patients (4%), titration was switched to the manual mode by the night staff, because high pressures >16 cmH_2O were delivered but not tolerated. In the event of a severe leak (>0.4 $L \cdot s^{-1}$) the mask was adjusted by the night staff or a chin strap was used to prevent leaking.

Treatment on the ward

If patients agreed, treatment was continued on the ward with a conventional fixed pressure CPAP device (Elite, ResMed, San Diego, CA, USA) as derived from the AutoSet®. Generally, the recommended pressure automatically calculated by the device (95th percentile pressure after excluding periods with leak >0.4 $L \cdot s^{-1}$) was used [18]. Heated humidification (HC 100, Fisher and Paykel, Auckland, New Zealand) was only added in patients who complained of nasal stuffiness, which they believed would preclude therapy. Patients were supervised on the ward for $\geqslant$1 week after titration. Prior to discharge, each patient decided

whether to continue CPAP treatment at home, which was defined as primary acceptance.

Wellbeing

In 41 unselected stroke patients with SDB, the effect of treatment on general subjective feeling was evaluated by the question "How fit do you feel in general?" and through use of a 100-mm visual analogue scale (VAS) from 0 (not fit at all) to 100 (completely fit). Differences in mm (ΔVAS) before and 10 days after initiation of treatment were compared in patients with (n=28) and without (n=13) primary nCPAP acceptance.

Twenty-four-hour blood pressure

In 16 unselected stroke patients with SDB, 24-h blood pressure measurement using a standard device (Tenso 24®, Speidel & Keller, Germany) was performed before and 10 days after initiation of CPAP treatment. The nondominant arm was used and the device was calibrated against a sphygmomanometer. If differences of >5 mmHg were found, the position of the microphone was adjusted. Differences in mean blood pressure during the day (from 07:00–22:00 h, every 15 min) and during the night (from 22:00–07:00 h, every 30 min) were compared between patients with and without treatment acceptance. "Nondippers" were defined as those with a nocturnal reduction in blood pressure of <10%. Existing antihypertensive medication was not changed during this time.

Statistics

Data are expressed as mean±SD. Descriptive statistics are given as mean and 95% confidence intervals. Differences between groups were analysed using the t-tests for either paired or unpaired comparisons as appropriate. Comparisons between groups were made using Fisher′s exact test. Logistic regression was performed with acceptance of CPAP as the dependent variable and age, sex, Epworth score, aphasia, Barthel index, RDI, minimal arterial oxygen saturation (S_{a,O_2}) and pressure as independent variables. A p-value <0.05 was considered significant.

Results

Effectiveness of treatment

Treatment with nCPAP was highly effective (table 3). There was a 80% reduction of respiratory events (RDI 38±20.9 untreated *versus* 7±7.1 h^{-1} treated, p<0.001) with a concomitant increase in oxygen saturation (minimal S_{a,O_2} 76+9.8 *versus* 89±4.6%, p<0.001), as expected. During titration nights, a significant increase in slow wave sleep (8.3±7.2 *versus* 12.5±10.9% of sleep period time (SPT), p<0.001), but not in rapid eye movement (REM) sleep (10.1±6.0 *versus* 10.9±6.3% SPT, p=0.206) was observed. There was a 40% reduction in the total arousal index (39.4±15.5 *versus* 22.9±10.2 h^{-1}, p<0.001) and a decrease in observed concomitant central apnoeas (2.9±4.9 *versus* 0.8±1.4 h^{-1}, p<0.001). Four patients (3.8%) rejected treatment during the titration night and in four other patients, automatic titration had to be switched to manual mode for some time due to high titration pressures (>16 cmH_2O), which were not well tolerated by the patients. Surprisingly, mouth leak did not appear to be a major problem.

Table 3. – Effects of treatment with nasal continuous positive airway pressure on sleep-disordered breathing and sleep stages

	Diagnostic	CPAP	p-value
RDI·h^{-1}	38±20.9	7±7.1	<0.001
Minimal S_{a,O_2} %	76.0±9.8	89.0±4.6	<0.001
Slow wave sleep SPT %	8.3±7.2	12.5±10.9	<0.001
REM SPT %	10.1±6.0	10.9±6.3	0.206
Arousal index·h^{-1}	39.4±15.5	22.9±10.2	<0.001
Central apnoea index·h^{-1}	2.9±4.9	0.8±1.4	<0.001

RDI: respiratory disturbance index; S_{a,O_2}: arterial oxygen saturation; SPT %: per cent of sleep period time; CPAP: continuous positive airway pressure.

Primary acceptance at the end of rehabilitation

Thirty-one of 105 patients (29.5%) rejected CPAP during the titration night or after a few nights on the ward. Reasons typically included mask discomfort or subjective sleep disturbances. In some cases no explanation was given. Seventy-four (70.5%) patients continued treatment at home.

Comparison of patients with and without continuous positive airway pressure acceptance

When comparing patients with and without primary acceptance, there was no difference in sex (male:female 57:17 *versus* 23:8, p=0.804), body mass index (BMI) (29±5.3 *versus* 28±4.5 $kg \cdot m^2$, p=0.447), subjective sleepiness prior to stroke (Epworth scale 7.2±4.8 *versus* 7.1±4.3, p=0.927), severity of SDB (RDI 38±19.9 *versus* 38±23.6 h^{-1}, p=0.940) or minimal S_{a,O_2} (75±10.5 *versus* 77±7.9%, p=0.505). The prescribed pressure on the ward was not different either (9.0±1.8 *versus* 8.6±2.0 cmH_2O, p=0.378). Patients accepting home CPAP therapy showed a better functional ability at the time of admission, as measured by the Barthel Index (81±25.4 *versus* 67±29.6, p=0.021), and there was a lower prevalence of symptoms of aphasia (8 *versus* 26%, p=0.012). They also tended to be younger (60±9.7 *versus* 63±7.8 yrs, p=0.082).

Logistical regression showed aphasic symptoms (coefficient b=-1.5126, p=0.026) and Barthel Index (b=0.0185, p=0.046) as the only significant predictors

Table 4. – Logistic regression predicting acceptance of treatment with continuous positive airway pressure

	B	p-value	OR (95% CI)
Aphasia	-1.5126	0.026	0.22 (0.06–0.83)
Barthel index	0.0185	0.046	1.02 (1.00–1.04)
Age	-0.0537	0.061	0.95 (0.90–1.00)

B: logistic regression coefficient; OR: odds ratio; CI: confidence interval.

of successful acceptance, with age of borderline significance (b=-0.054, p=0.061, table 4).

There was neither a difference in type of stroke (bleeding or ischaemic with the subgroups of cardiac, large vessel, small vessel, other but determined origin, and unknown origin) or the site of lesion (left or right, hemispheric or brainstem). Similarly, average mouth leak during sleep was not a determinant of primary acceptance (data not shown).

Effects of continuous positive airway pressure on subjective wellbeing

The 41 patients investigated for wellbeing did not differ from the rest of the study population in age, BMI, RDI, minimal Sa,O_2, Epworth score, CPAP pressure requirement, days after stroke, or Barthel Index (all comparisons nonsignificant). Using a visual analogue scale, those with CPAP acceptance (n=28) showed an improvement in wellbeing (ΔVAS 26±26.3 mm), whereas those without acceptance (n=13) did not (ΔVAS 2±25.1 mm, p=0.021, fig. 1).

Effects on twenty-four-hour blood pressure

The 16 patients that underwent 24-h blood measurements before and 10 days after initiation of CPAP treatment did not differ from the total group regarding clinical, polysomnographic, and neurological data.

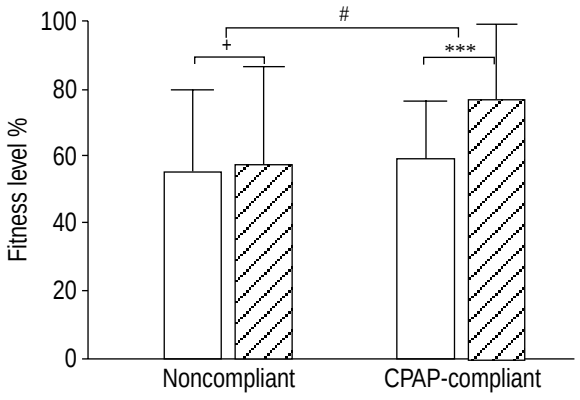

Fig. 1. – Effects of treatment with nasal continuous positive airway pressure on subjective wellbeing, measured by a visual analogue scale (0: not fit at all; 100: 100 per cent), in patients compliant and noncompliant with continuous positive airway pressure (CPAP) during rehabilitation. □: before; ▨: after 10 days. #: p=0.021; +: p=0.762; ***: p<0.001.

Furthermore, there was no difference in systolic or diastolic blood pressure, defined as the mean of three standardized conventional measurements on the ward during the day (systolic 131±13.0 *versus* 133±18.0 mmHg, diastolic 76±6.3 *versus* 79±9.7 mmHg).

Eleven patients showed a high compliance (usage time 6.9±1.5 $h \cdot night^{-1}$), whereas five patients did not use CPAP (usage time 0.4±0.6 $h \cdot night^{-1}$). The five noncompliant patients were less obese (BMI 25±1.8 *versus* 30±4.8 $kg \cdot m^2$, p=0.04) and tended to be older (63±5.0 *versus* 57±10.3 yrs, p=0.12). There was no difference in severity of OSA between the two groups (RDI 34±20 *versus* 44±22, p=0.414). Four of five noncompliant patients and eight of 11 compliant patients had a history of hypertension. Ten days after initiation of CPAP therapy there was a significant reduction in mean nocturnal arterial blood pressure (ΔBP -8±7.3 mmHg) in the compliant stroke patients but virtually no pressure change in the noncompliant group (ΔBP 0.8±8.4 mmHg, p=0.037). After 10 days of treatment, four of the 11 compliant patients were classified as overnight blood pressure "dippers", whereas none of the five noncompliant patients showed dipping during the night. In both groups, there was no difference in mean blood pressure during the day (ΔBP -4.3±8.4 *versus* -6.8±5.6 mmHg, p=0.570).

Discussion

nCPAP is the most effective and widely used therapy for OSA. The present study demonstrates, in a neurorehabilitation setting, that moderate-to-severe OSA after stroke can be treated effectively with CPAP, with clear improvements in both sleep and breathing. Using an autotitration approach followed by fixed-pressure treatment, primary CPAP acceptance was good, although not excellent given the degree of coaching. Ten days of nCPAP produced a large improvement in subjective wellbeing and a reduction in mean nocturnal blood pressure in compliant patients.

Sleep architecture

An interesting observation of the present study was the rebound of slow wave sleep rather than of REM sleep. In OSA patients there is typically a large increase in REM and slow wave sleep on the first treatment night [18]. The reason for the lack of REM rebound in the present subjects is not clear, since both REM sleep and, to a lesser extent, slow wave sleep were reduced in the patients with SDB compared to those without [3]. One possible explanation is that the stroke itself altered central sleep mechanisms. The overall number of arousals decreased, but not to the extent of the reduction of respiratory events, which indicates other causes of sleep fragmentation besides OSA in this population. Moreover, the polysomnographic results of sleep architecture should not be overinterpreted from a single diagnostic and a single titration night; adaptation nights were not performed in the sleep laboratory.

Titration procedure and follow-up

The procedure used in the study is somewhat different to the recommended CPAP titration performed in the sleep apnoea population without stroke. Usually, patients are diagnosed as having OSA on one night and manually titrated on a subsequent night, with discharge the next day. Attended autotitration was used, followed by intensive supervision in the rehabilitation unit. The efficacy of autotitration with AutoSet® and the suitability of the low-leak 95th-percentile pressure for fixed pressure CPAP treatment used in the present setting has recently been confirmed by others [19]. This titration procedure allowed for quantification of the total leak. No significant difference was found between the severity of leak in stroke patients with and without primary acceptance, indicating that leakage does not play a major role in treatment acceptance. Stroke patients at the Fachklinik Rhein/Ruhr routinely had 3–4 weeks hospitalization during neurological rehabilitation. This allowed for close supervision, which included almost daily visits, adjustment of mask fittings, and repeated explanations during the first week, followed by close supervision thereafter, as recommended by Hoy *et al.* [20]. It is not known what acceptance would have been achieved without this intensive coaching, but it is the authors' impression that such coaching is required in this group in order to achieve adequate acceptance and compliance.

Acceptance

As with any chronic therapy, long-term compliance has a significant impact on its effectiveness. CPAP acceptance in patients with simple moderate-to-severe OSA is reported to range between 70–80% [21, 22]. The present study demonstrates that an almost similar level of early acceptance can be achieved in selected stroke patients with a similar degree of OSA. Compliers and noncompliers did not differ in their baseline characteristics (anthropometric data, severity of OSA) and subjective sleepiness assessed by the Epworth Sleepiness Scale. The only significant predictors of successful acceptance were the presence of aphasia (negative predictor) and the severity of motor disability as quantified by the Barthel Index (also a negative predictor). For example, the odds ratio for aphasia showed that it was associated with only 22% of the acceptance rate of a stroke patient with a similar degree of OSA without aphasic symptoms. It might be speculated that the presence of aphasia could be related to inability to understand the potential benefits or to subjectively evaluate a change in sleepiness on therapy. This might partially explain the higher failure rate reported by others when CPAP was initiated early after stroke onset. In simple OSA, long-term compliance appears to be related to the initial severity of daytime symptoms related to alertness and performance, and in particular to the degree of daytime sleepiness. There is evidence that up to 90% of symptomatic patients with successful primary acceptance continue to use CPAP in the long term [23]. This is by no means certain in the present population, since subjective sleepiness was not a major problem in the stroke population with SDB. Therefore, a somewhat higher dropout rate might be expected during follow-up visits. However, this point should not be overemphasized as the Epworth scale is known to be of limited value in this setting [24].

Patients with less severe OSA experiencing nasal and pharyngeal side-effects or those showing no improvement after CPAP are most likely to discontinue treatment [25]. It is, therefore, believed that intensive coaching during the first weeks of treatment is of crucial importance to maintain a high compliance.

Improvement in wellbeing

In a subgroup of stroke patients a VAS was used to investigate the effect of nCPAP on subjective wellbeing. This was a random sample that did not differ from the remaining study population. The results derived from this analogue scale suggest that effective CPAP therapy improves subjective wellbeing of stroke victims with SDB. The degree of improvement may be similar to the effects on mood and cognitive function reported in sleep apnoea patients without stroke [26]. A VAS is used in psychological research to detect changes in mood and subjective activation [27]. Although this relatively simple measurement was used, these results suggest that some of the cognitive deficits usually attributed to cerebrovascular accidents might be due to undiagnosed sleep disordered breathing. However, this speculation needs to be proven by appropriate neuropsychological testing using well-validated instruments. It is noteworthy that all staff (*e.g.* physiotherapists, ergotherapists *etc.*) perceived that these patients responded to rehabilitation better when receiving effective nCPAP therapy.

Blood pressure

The present study suggested, for the first time in stroke patients that even 10 days of treatment of OSA with nCPAP may produce a substantial drop in mean night-time blood pressure. Some of the CPAP users were essentially converted from "nondippers" to nocturnal "dippers". It should be stressed that according to the responsible physician, these patients were on optimal antihypertensive therapy. Thus, treatment with nCPAP may have a clear effect on nocturnal arterial blood pressure. One of the patients was a 36-yr-old male with intracranial hypertensive bleeding, in whom reasonable blood pressure adjustment had not been achieved with five different antihypertensive agents. After diagnosis of OSA and treatment with nCPAP, normal diurnal rhythm of blood pressure was restored and pressure could be easily adjusted with less medication [28]. CPAP might cause an unwanted drop in blood pressure in these already highly medicated patients. Although this did not happen in the present population, it should be considered in patients who require maximal

antihypertensive therapy. Similar results on night-time blood pressure as in the present study have been recently been reported after correction of SDB in patients with hypertension [29]. Since hypertension refractory to medical therapy and elevated nocturnal blood pressure carry a high vascular risk in patients with hypertension, lowering of nocturnal blood pressure could potentially improve the prognosis of stroke patients with SDB. It has been demonstrated that even a diastolic blood pressure remaining 5 mmHg above the age-related target pressure is associated with an increased likelihood of stroke [30]; prolonged differences in diastolic blood pressure of 5, 7.5, and 10 mmHg, respectively, were associated with at least 34%, 46%, and 56% less stroke [31]. Therefore, lowering the elevated blood pressure in stroke is one of the key management principles of secondary prevention and, therefore, recognition and treatment of significant OSA should be part of standard stroke management.

It is concluded that nasal continuous positive airway pressure is an effective, safe and important therapeutic option in stable stroke patients with moderate-to-severe obstructive sleep apnoea. In the present population, primary acceptance was similar to that in patients with simple obstructive sleep apnoea. Continuous positive airway pressure acceptance was associated with improved subjective wellbeing and decreased nocturnal blood pressure, which may improve prognosis in stroke patients. Its role in the first month or two after the acute event remains to be investigated.

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