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Flexible Positive Airway Pressure Improves Treatment Adherence Compared with Auto-adjusting PAP

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Study Objectives: There are no clinical data comparing adherence and quality of life between auto-adjusting positive airway pressure (APAP) and two different flex positive airway pressure (PAP) devices (A-Flex, C-Flex) in patients with obstructive sleep apnea (OSA).

Design and Setting: Ninety-three patients in whom OSA was newly diagnosed were randomly assigned to receive 3 mo of APAP (n = 31), APAP with C-Flex (n = 31), or APAP with A-Flex (n = 31). Objective adherence was determined after 3 mo of CPAP treatment, and the Epworth Sleepiness Scale (ESS), Pittsburgh Sleep Quality Index (PSQI), and Calgary Sleep Apnea Quality of Life Index (SAQLI) were examined at baseline and after 3 mo. After 3 mo, patients in the APAP with A-Flex group and those in the APAP with C-Flex group were crossed over and those in the APAP group were switched to A-Flex for an additional 3 mo.

Measurements and Results: The groups were similar demographically. Treatment adherence during the first 3 mo was significantly greater in the APAP with C-Flex group (APAP with C-Flex: 5.19 ± 1.84 h/night versus APAP: 3.96 ± 1.66 h/night versus APAP with A-Flex: 4.27 ± 2.12 h/night, P = 0.04). There was a significant improvement in two of four of the SAQLI domain scores and in the ESS and PSQI in the APAP with C-Flex group. Adherence significantly improved among the poor compliers (< 4 h/night of use) in the APAP group after change to APAP with A-Flex (P = 0.01).

Conclusions: Of these three modes of PAP delivery, adherence was greatest with APAP with C-Flex.

Clinical Trial Registration: URL: http://www.clinicaltrials.gov. Unique identifier: NCT00873977.

Keywords: A-Flex, C-Flex, continuous positive airway pressure, obstructive sleep apnea, treatment adherence

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INTRODUCTION

Continuous positive airway pressure (CPAP), the mainstay of treatment for moderate to severe obstructive sleep apnea (OSA), has been shown to normalize sleep architecture, reduce daytime sleepiness, enhance daily function, and decrease cardiovascular events.[1-3] Although CPAP is a highly effective treatment, adherence is suboptimal. To improve patient comfort and treatment adherence, various CPAP modalities have been developed. Auto-adjusting positive airway pressure (APAP) devices continuously adjust the pressure in real time according to that required to maintain upper airway patency. It has been reported that treatment compliance with APAP was equivalent to that with fixed PAP therapy.[4-6] Adherence with flexible CPAP (C-Flex; Philips Respironics, Murraysville, PA, USA), which flexes airway pressure on exhalation and inhalation on a breath-by-breath basis to reduce the work of breathing, has been reported to be significantly better compared with fixed PAP therapy in one study.[7] However, other studies reported that adherence with C-Flex and fixed positive airway pressure (PAP) therapy was similar.[8-11] To our knowledge, a comparison of treatment adherence of APAP with APAP with C-Flex has not been reported. Because the use of APAP for the treatment of OSA has increased, a prospective randomized study comparing APAP to APAP with C-Flex with respect to CPAP adherence is needed. In addition, a new CPAP device (A-Flex; Philips Respironics) is designed to further improve breathing comfort. Like C-Flex, A-Flex flexes pressure at the beginning of exhalation but also has a fixed 2 cm H_2O pressure difference between inspiration and expiration.

The aim of this study was to compare objective adherence to CPAP between APAP, APAP with C-Flex, and APAP with A-Flex over an initial 3-mo period. We also investigated daytime sleepiness, sleep quality, and quality of life (QOL). Additionally, after 3 mo, patients in the APAP with A-Flex group and the APAP with C-Flex groups were crossed over to use the alternate mode (C-Flex or A-Flex) to compare adherence. In addition, the APAP group was crossed over to the A-Flex for these final 3 mo.

METHODS

Study Participants

Patients in whom OSA was newly diagnosed (apnea-hypopnea index [AHI] > 20) were enrolled in the current study according to the Japanese Health Insurance System. Patients were excluded if they were younger than 20 y, had a major medical or psychiatric condition that would interfere with the demands of the study and adherence to PAP, or had ever used CPAP therapy. This study was approved by the Ethics Committee of Kyoto University. All patients gave written informed consent to participate.

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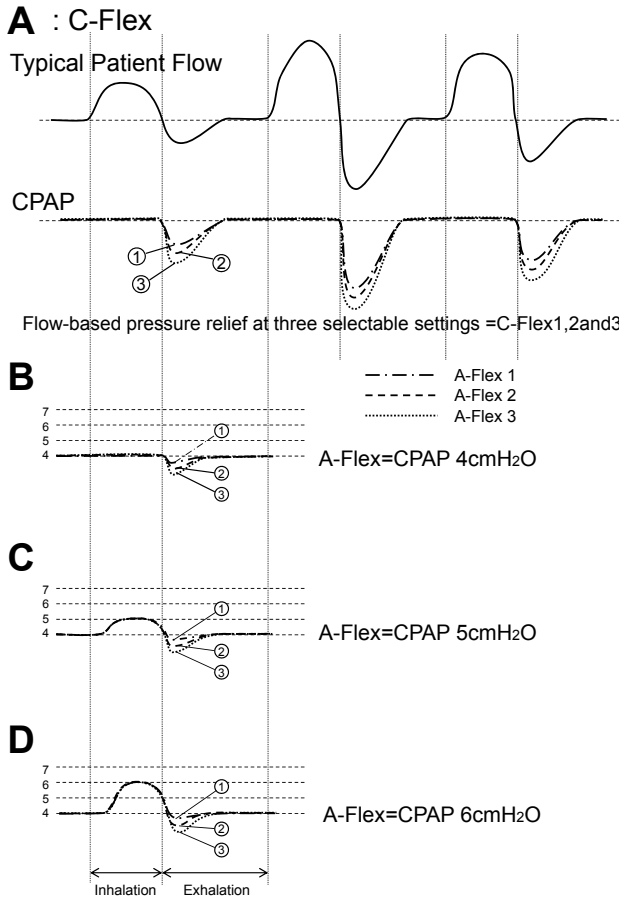

Figure 1—(A) C-Flex pressure relief reduced pressure at the beginning of exhalation and returned to the therapeutic pressure just before inhalation. The level of pressure relief varies based on the patient's expiratory flow and which of the three C-Flex settings (1, 2, and 3) has been selected. **(B-D)** A-Flex has the same function as C-Flex during expiration. At 4 cm H_2O CPAP, the A-Flex PAP machine is same as the C-Flex machine PAP **(B)**. At 5 cm H_2O CPAP, the A-Flex PAP machine can provide 1 cm H_2O pressure support at the inspiration **(C)**. From 6 or more cm H_2O CPAP, A-Flex machine can make 2 cm H_2O pressure supports at the inspiration **(D)**.

C-Flex and A-Flex PAP Machines

C-Flex pressure relief was developed to make CPAP therapy more comfortable by reducing pressure at the beginning of exhalation and returning to the therapeutic pressure just before inhalation (Figure 1A). The level of pressure relief varies based on the patient's expiratory flow and which of the three C-Flex settings (1, 2, and 3) has been selected.

Like C-Flex, A-Flex provides flow-based pressure relief at the beginning of exhalation. At 4 cm H_2O CPAP, the A-Flex PAP machine is the same as the C-Flex machine PAP (Figure 1B). However, at 5 cm H_2O CPAP, the A-Flex PAP machine can provide 1 cm H_2O pressure support at inspiration (Figure 1C). From 6 cm or more H_2O CPAP, the A-Flex machine can provide 2 cm H_2O pressure support at inspiration (Figure 1D). A-Flex has the same function as C-Flex during expiration (Figure 1B-D).

Study Design

The study was a randomized single-blind (patients blinded) crossover trial of APAP versus APAP with C-Flex (set to dip level 3) versus APAP with A-Flex (set to dip level 3). The dip level is the level of pressure reduction during expiration, and dip level 3 is the greatest pressure reduction during expiration. Data were collected at baseline and after 3 and 6 mo of PAP treatment. At baseline, we recorded the patients' demographic characteristics and polysomnographic data. In addition, subjective sleepiness, sleep quality, and health-related QOL were measured using the Epworth Sleepiness Scale (ESS),[12] Pittsburgh Sleep Quality Index (PSQI),[13] and Calgary Sleep Apnea Quality of Life Index (SAQLI).[14,15] The SAQLI consists of five domains: daily functioning (domain A), social interactions (domain B), emotional functioning (domain C), symptoms (domain D), and treatment-related symptoms (domain E). The total SAQLI score for domains A through D was obtained before and after CPAP treatment, and the score for domain E was factored in after the patient received CPAP. CPAP titration was performed with autotitration during full-night polysomnography (PSG) attended by sleep technicians and the pressure range was between 4 and 20 cm H_2O. For CPAP titration, each patient underwent full-night PSG on the allocated CPAP mode (i.e., APAP with C-Flex group underwent full-night PSG on APAP with C-Flex). The attending technicians checked for abnormal movements of the titrated PAP machine. However, they could not find any trouble during this trial.

The primary outcome was objective adherence after 3 mo of CPAP treatment. Objective adherence was downloaded from the memory card (Encore Pro Smartcard; Philips-Respironics) located in the PAP device. Secondary outcomes were ESS, PSQI, and SAQLI at 3 mo after the beginning of CPAP treatment.

Additionally, after 3 mo of PAP treatment, the APAP with A-Flex group and the APAP with C-Flex group were crossed over to the alternate mode (C-Flex or A-Flex) and the APAP group was switched to A-Flex for an additional 3 mo. The evaluations performed at 3 mo were repeated 6 mo after the start of CPAP treatment.

Polysomnography

The diagnosis of OSA was confirmed by PSG (SomnoStar Pro, Cardinal Health, Dublin, OH, USA), which was started at 22:00 and ended at 6:00 the following morning. Surface electrodes were attached using standard techniques to obtain an electrooculogram, electromyogram of the chin, and 12-lead electroencephalograph. Sleep stages were defined according to the criteria of Rechtschaffen and Kales.[16] Ventilation/respiratory effort was monitored by inductive plethysmography (Respitrace QDC, Viasys Healthcare, Palm Springs, CA, USA). Airflow was monitored by a nasal pressure transducer (PTAFlite, Pro-Tech Services Inc., Mukilteo, WA, USA) and supplemented by an oronasal thermal sensor (Sleepmate Technologies, Midlothian, VA, USA). Arterial oxygen saturation (SaO_2) was monitored continuously with a pulse oximeter (Adult Flex System, Nonin Medical, Plymouth, MN, USA).

Apnea was defined as the complete cessation of airflow and hypopnea as a clear decrease in airflow of 50% or more lasting for 10 sec or more accompanied by a decrease in SpO_2 of at least 3% and/or associated with arousal.[17] All AHI values were expressed as the number of episodes of apnea and hypopnea per h over the total sleep time. The lowest SpO_2 during sleep was calculated in each patient.

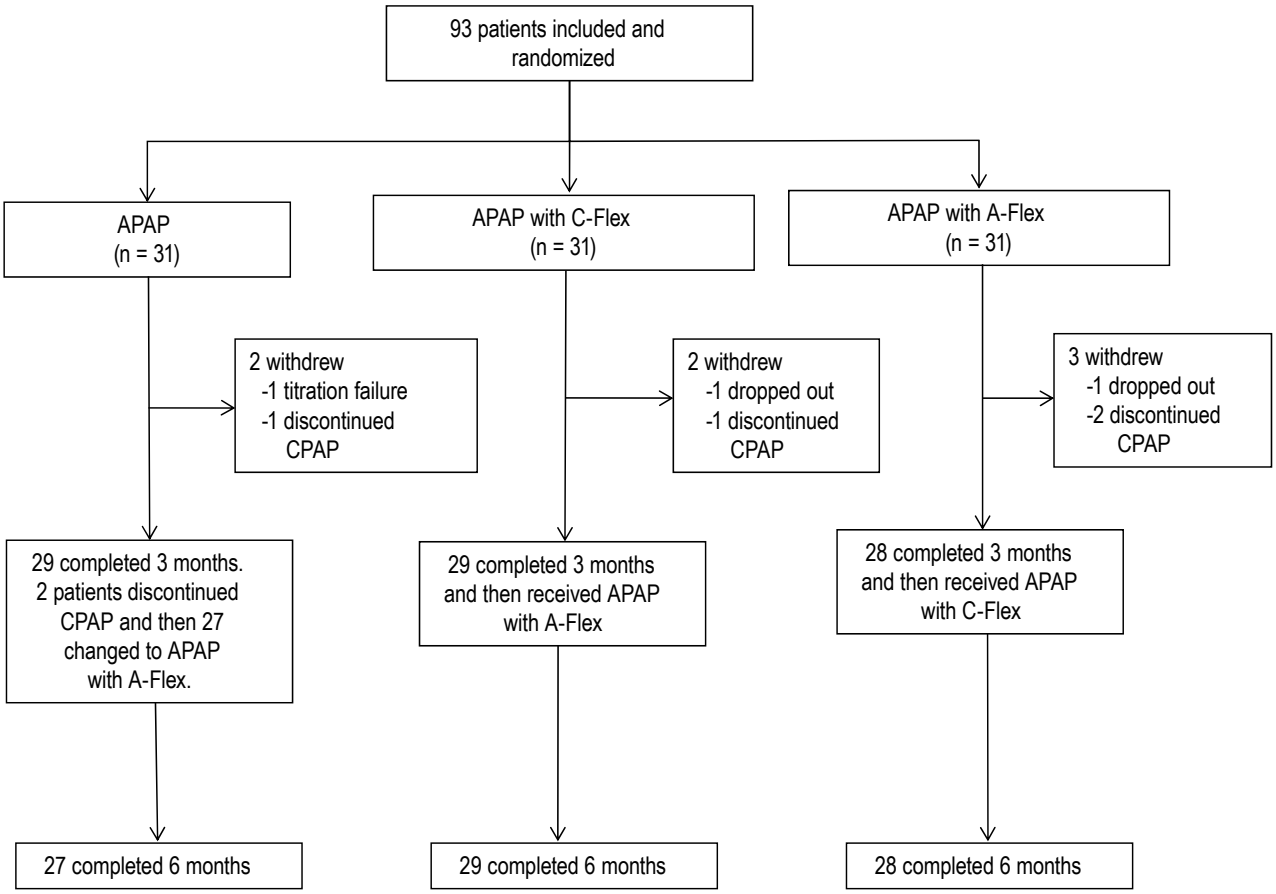

Figure 2—Flow chart of the study population. APAP, auto-adjusting positive airway pressure; CPAP, continuous positive airway pressure.

Randomization

This study was randomized via blinded envelope prior to the beginning of the study.

Power Analysis

Based on a previous study,[7] differences of 1 h/night of PAP adherence between each group were decided to be clinically significant, and standard deviation (SD) of 1.5 h/night was expected. The sample size was set to achieve 80% power at a 5% significance level. The calculated sample size in each group was 36 patients.

Statistical Analysis

Data analysis was conducted using a statistical software program (Statview, version 5.0; SAS Institute Inc., Cary, NC, USA). Data were expressed as mean ± SD or absolute numbers and percentages in each study group. The patients' demographic characteristics, polysomnographic data, responses to three questionnaires at baseline and after 3 mo of CPAP treatment, and adherence after 3 mo of CPAP treatment were compared among the three groups using a one-way analysis of variance. When a significant difference was observed, we used the Bonferroni/Dunn method to identify where the differences were significant. For categorical variables, the χ^2 test was used. Within the group, comparisons of adherence (3 mo versus 6 mo) or of results from the three questionnaires (baseline versus 3 mo, 3 mo versus 6 mo) were analyzed using a paired *t* test. In all analyses, $P < 0.05$ was considered statistically significant.

RESULTS

Baseline Assessments

Figure 2 shows the study flow chart. Ninety-three patients in whom OSA was newly diagnosed were randomly assigned to receive 3 mo of APAP (n = 31), APAP with C-Flex (n = 31), or APAP with A-Flex (n = 31). During the first 3 mo, two patients withdrew from the APAP group (one discontinued PAP, one had Cheyne-Stokes breathing during PAP titration), two patients withdrew from the APAP with C-Flex group (one dropped out, one discontinued PAP), and three patients withdrew from the APAP with A-Flex group (one dropped out, two discontinued PAP). Data on patients who dropped out during the first 3 mo were excluded from the analysis.

Tables 1 and 2 summarize baseline characteristics and polysomnographic data, respectively, on study participants. Patients were predominantly male, middle-aged, and had moderate to severe OSA. Neither baseline characteristics nor polysomnographic data differed among the three groups.

Effects of CPAP Treatment on PSG Variables

Table 3 shows the polysomnographic data on the PAP night. Compared with the baseline PSG, significant changes in polysomnographic variables such as the AHI and arousal index were

Table 1—Baseline characteristics of study participants[a]

	All (n = 86)	APAP (n = 29)	APAP with C-Flex (n = 29)	APAP with A-Flex (n = 28)	P value
Age (y)	59.3 ± 10.8	56.9 ± 8.8	61.0 ± 10.7	59.8 ± 12.6	0.33
Sex (male/female)	72/14	25/4	24/5	23/5	0.90
BMI (kg/m^2)	27.1 ± 4.7	27.4 ± 5.5	27.4 ± 4.2	26.6 ± 4.4	0.77
Living alone	11 (12.8)	6 (20.7)	3 (10.3)	2 (7.1)	0.29
Hypertension	50 (58.1)	14 (48.3)	20 (69.0)	16 (57.1)	0.28
Dyslipidemia	42 (48.8)	14 (48.3)	13 (44.8)	15 (53.6)	0.80
Diabetes mellitus	27 (31.4)	11 (37.9)	7 (24.1)	9 (32.1)	0.52
ESS	9.2 ± 4.4	9.5 ± 4.6	9.2 ± 4.5	8.9 ± 4.3	0.88

[a]Mean ± SD or number (%). APAP, auto-adjusting positive airway pressure; BMI, body mass index; ESS, Epworth Sleepiness Scale.

Table 2—Baseline polysomnographic data on study participants[a]

	APAP (n = 29)	APAP with C-Flex (n = 29)	APAP with A-Flex (n = 28)	P value
Sleep efficiency, %	75.1 ± 11.9	72.2 ± 12.7	70.6 ± 15.0	0.43
S1, %	26.6 ± 13.7	26.8 ± 14.2	27.2 ± 14.2	0.98
S2, %	52.0 ± 11.8	54.2 ± 13.5	52.7 ± 11.0	0.78
S3/4, %	6.4 ± 8.9	4.4 ± 6.2	6.3 ± 8.6	0.57
REM, %	15.0 ± 5.0	14.6 ± 5.0	13.9 ± 6.7	0.73
Arousal, events/h	34.1 ± 12.4	36.3 ± 14.7	36.2 ± 14.2	0.79
Central apnea, events/h	2.9 ± 5.0	2.3 ± 3.7	3.3 ± 5.2	0.69
AHI, events/h	40.8 ± 12.4	43.3 ± 15.2	45.7 ± 15.9	0.46
Mini SpO_2 (%)	77.0 ± 7.4	75.2 ± 12.8	78.4 ± 6.5	0.44
SpO_2 < 90% (% TST)	16.2 ± 14.9	14.9 ± 16.6	18.4 ± 23.2	0.77

[a]Mean ± SD or number (%). AHI, apnea-hypopnea index; APAP, auto-adjusting positive airway pressure; REM, rapid eye movement; SpO_2, percutaneous oxygen saturation; TST, total sleep time.

Table 3—Polysomnographic data on study participants upon CPAP titration[a]

	APAP (n = 29)	APAP with C-Flex (n = 29)	APAP with A-Flex (n = 28)	P value
Sleep efficiency, %	77.2 ± 11.4	76.5 ± 7.9	72.0 ± 11.5	0.14
S1, %	15.7 ± 7.7	16.2 ± 9.9	16.9 ± 9.5	0.89
S2, %	57.3 ± 8.0	60.7 ± 11.8	57.1 ± 9.3	0.29
S3/4, %	6.9 ± 8.3	4.4 ± 5.3	6.6 ± 7.3	0.34
REM, %	20.1 ± 5.0	18.7 ± 6.1	19.5 ± 5.8	0.63
Arousal, events/h	20.2 ± 9.0	19.7 ± 9.4	20.7 ± 9.7	0.93
Central apnea, events/h	1.4 ± 1.6	1.4 ± 1.8	2.5 ± 2.9	0.09
AHI, events/h	4.0 ± 3.7	3.8 ± 4.7	6.0 ± 4.5	0.11
Mini SpO_2 (%)	90.2 ± 3.9	87.5 ± 9.4	88.8 ± 4.5	0.27
SpO_2 < 90% (% TST)	0.2 ± 0.6	2.1 ± 6.2	1.2 ± 4.8	0.30

[a]Mean ± SD or number (%). AHI, apnea-hypopnea index; APAP, auto-adjusting positive airway pressure; CPAP, continuous positive airway pressure; REM, rapid eye movement; SpO_2, percutaneous oxygen saturation; TST, total sleep time.

noted in all three groups. There were no significant differences among the three groups in the polysomnographic data on CPAP titration. Also, the number of patients who used hypnotic agents during CPAP titration did not differ significantly among the three groups (APAP with C-Flex: 7 of 29, 24.4% versus APAP: 11 of 29, 37.9% versus APAP with A-Flex: 9 of 28, 32.1%; P = 0.52).

After 3 mo of treatment, the 90th percentile PAP, leak, and mean AHI were downloaded and recorded from the memory card located in the PAP device. There were no significant differences among the three groups in terms of residual AHI (APAP with C-Flex: 3.4 ± 2.2 events/h versus APAP: 3.5 ± 2.0 h/night versus APAP with A-Flex: 4.6 ± 2.9 h/night; P = 0.11), 90th percentile PAP (APAP with C-Flex: 8.4 ± 1.7 cm H_2O versus APAP: 8.2 ± 1.3 cm H_2O versus APAP with A-Flex: 8.8 ± 1.7 cm H_2O; P = 0.32), or 90th percentile leak (APAP with C-Flex: 45.7 ± 7.0 L/min versus APAP: 49.7 ± 13.1 L/min versus APAP with A-Flex: 46.5 ± 11.5 L/min; P = 0.34).

Primary Outcome: Adherence Over 3 Mo

Figure 3 shows a comparison among the three groups with regard to adherence to CPAP treatment over a 3-mo period. Median adherence was significantly greater in the APAP with C-Flex group, especially compared with the APAP group (APAP with C-Flex, n = 29: 5.19 ± 1.84 h/night versus APAP, n = 292 9: 3.96 ± 1.66 h/night versus APAP with A-Flex, n = 28: 4.27 ± 2.12 h/night; P = 0.04). In the *post hoc* analysis, adherence to APAP with C-Flex was significantly greater in comparison with APAP (P = 0.01). In addition, there were significant differences among the groups in percentage of days PAP was used (APAP with C-Flex: 91.9 ± 10.6% versus APAP: 79.4 ± 21.8% versus APAP with A-Flex: 82.5 ± 22.9%; P = 0.04) but not in percentage of days PAP used > 4 h (APAP with C-Flex: 66.6 ± 29.8% versus APAP: 54.8 ± 27.9% versus APAP with A-Flex: 57.6 ± 32.7%; P = 0.30). *Post hoc* testing revealed that the percentage of days PAP was used in the APAP with C-Flex group was significantly higher than in the APAP group (P = 0.02).

Secondary Outcomes: ESS, PSQI, and SAQLI After 3 Mo of CPAP Treatment

Table 4 details the effect of CPAP treatment on ESS, PSQI, and SAQLI in the three groups. For the entire group, ESS (P = 0.004) and domain A (P = 0.04), domain C (P = 0.006), and domain D (P < 0.0001) in the SAQLI questionnaire were significantly improved after 3 mo of PAP. Differences in responses to these three questionnaires were not statistically significant among the three groups at baseline, but after 3 mo of PAP treatment differences were noted. ESS and PSQI scores were significantly improved using APAP with C-Flex (ESS, 9.2 ± 4.5 to 7.3 ± 3.8, P = 0.01; PSQI, 7.2 ± 3.6 to 6.1 ± 2.8, P = 0.04), whereas significant improvements with APAP and APAP with A-Flex were not observed. In the SAQLI questionnaire, two domains were significantly improved and the other two domains trended toward improvement in the APAP with C-Flex group. On the other hand, the APAP and APAP with A-Flex groups had a significant improvement only in one domain of the SAQLI. However, as to the changes in the values for ESS, PSQI, and SAQLI among the three groups between before and after 3 mo of CPAP, the APAP with C-Flex group tended to have greater improvement in PSQI (P = 0.08) than the other two groups, whereas differences in the ESS and SAQLI were not significantly different among the three groups (Table 5).

Crossover in CPAP Mode

After 3 mo, two patients discontinued PAP treatment in the APAP group. The change in the CPAP mode did not have a significant effect on PAP adherence in any group (from APAP to APAP with A-Flex, n = 27, from 4.15 ± 1.51 h/night to 4.12 ± 1.16 h/night, P = 0.89; from APAP with C-Flex to APAP with A-Flex, n = 29, from 5.19 ± 1.84 h/night to 4.95 ± 1.94 h/night, P = 0.17; from APAP with A-Flex to APAP with C-Flex, n = 28, from 4.27 ± 2.12 h/night to 4.15 ± 1.99 h/night, P = 0.56). Although the group of patients moving from APAP to APAP with A-Flex tended to show improvement in domain B of the SAQLI (P = 0.07), ESS, PSQI, and SAQLI scores did not significantly change in any group (results not shown).

In a subgroup analysis of poor compliers (< 4 h/night of PAP use), there was a significant increase in PAP adherence in the patients moving from APAP to APAP with A-Flex (n = 10, from 2.55 ± 0.76 h/night to 3.20 ± 0.85 h/night, P = 0.01) (Figure 4). In contrast, adherence did not change between 3 and 6 mo in the other groups.

DISCUSSION

The current study is the first to show a significant superiority of APAP with C-Flex on treatment adherence during the first 3 mo of use compared with APAP. Also, only patients using APAP with C-Flex had a significant improvement in subjective sleepiness and sleep quality. These results suggest that APAP with C-Flex may be a superior CPAP modality for the initial treatment of moderate to severe OSA.

To date, it has not been shown that PAP adherence can be improved by using different pressure applications of PAP. A meta-analysis of a number of published studies comparing

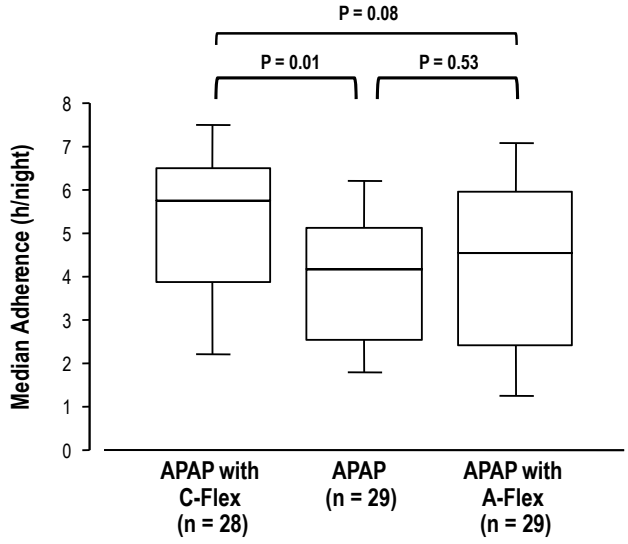

Figure 3—CPAP adherence with APAP with C-Flex, APAP, and APAP with A-Flex after 3 mo of treatment. Data are shown as a bow-whisker plot with median and 25th percentile of CPAP adherence. APAP, auto-adjusting positive airway pressure.

Table 4—Analysis of health-related quality of life and sleep related questionnaires[a]

	APAP (n = 29)			C-Flex (n = 29)			A-Flex (n = 28)		
	BL	3 mo	P value	BL	3 mo	P value	BL	3 mo	P value
ESS	9.5 ± 4.6	8.2 ± 4.0	0.12	9.2 ± 4.5	7.3 ± 3.8[b]	0.01	8.9 ± 4.3	8.1 ± 4.3	0.34
PSQI	6.0 ± 2.5	6.1 ± 2.9	0.72	7.2 ± 3.6	6.1 ± 2.8[b]	0.04	6.3 ± 3.2	5.8 ± 2.3	0.21
SAQLI									
Domain A	5.6 ± 1.1	5.7 ± 1.2	0.56	5.2 ± 1.3	5.5 ± 1.1[c]	0.08	5.4 ± 1.1	5.6 ± 1.3	0.37
Domain B	5.6 ± 0.9	5.7 ± 1.0	0.70	5.3 ± 1.1	5.7 ± 1.0[b]	0.02	5.8 ± 1.1	5.8 ± 0.8	0.89
Domain C	5.1 ± 0.9	5.3 ± 1.1	0.11	4.9 ± 1.0	5.2 ± 1.0[c]	0.06	5.1 ± 0.9	5.3 ± 0.9	0.26
Domain D	2.7 ± 1.1	3.7 ± 1.4[b]	0.0009	2.6 ± 1.2	3.5 ± 1.6[b]	0.001	2.3 ± 1.2	3.8 ± 1.7[b]	< 0.0001
Domain E		4.7 ± 1.2			4.3 ± 1.1			4.6 ± 1.2	
Total	4.8 ± 0.7	4.7 ± 1.2	0.71	4.5 ± 0.8	4.5 ± 1.1	0.83	4.7 ± 0.7	4.8 ± 1.1	0.65

[a]Mean ± SD. [b]P < 0.05 versus BL. [c]P < 0.10 versus BL. APAP, auto-adjusting positive airway pressure; BL, baseline; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; SAQLI, Calgary Sleep Apnea Quality of Life Index. Domain A, daily functioning; Domain B, social interactions; Domain C, emotional functioning; Domain D, symptoms; Domain E, treatment-related symptoms.

APAP with fixed CPAP revealed that there was no difference between the two modalities regarding subjective sleepiness and adherence to PAP.[4,18] The difficulty of exhaling against a fixed positive pressure is a common complaint when using CPAP, so C-Flex was developed, which reduces pressure at the beginning of exhalation and increases pressure to a level determined to be therapeutic for the latter part of exhalation. Aloia et al.[7] demonstrated that use of a C-Flex device provided a significant improvement in CPAP adherence (1.7 h/night of additional use after a 12-wk follow-up period compared with a fixed PAP therapy). However, this study was not a randomized trial. Thereafter, Marshall et al.[19] reported that in a 4-wk randomized study there was a trend toward greater CPAP adherence with C-Flex compared with fixed PAP therapy (C-Flex, 4.7 ± 2.9 h/night versus fixed PAP, 3.0 ± 2.1 h/night), but the difference was not statistically significant because of the small sample size. A meta-analysis also found that C-Flex does not provide any significant benefit over fixed PAP in terms of treatment adherence.[20]

In the current study, we confirmed that APAP with C-Flex was associated with significantly greater CPAP adherence than APAP. Many studies suggested that APAP reduces the mean PAP requirements, which are thought to influence CPAP adherence.[4-6] C-Flex is designed to flexibly deliver pressure on a breath-by-breath basis by adjusting pressure within exhalation, which may be a more important variable for treatment adherence than the overall PAP level. This C-Flex technology may be responsible for the significant superiority of treatment adherence with APAP with C-Flex compared with APAP. Our study also showed that adherence in the APAP with A-Flex group did not improve after changing to the use of APAP with

Table 5—Changes in values of ESS, PSQI, and SAQRI among the three groups from before and after 3 mo of CPAP[a]

	APAP (n = 29)	APAP with C-Flex (n = 29)	APAP with A-Flex (n = 28)	P value
ESS	-1.3 ± 4.3	-2.2 ± 3.9	-0.8 ± 4.3	0.45
PSQI	0.2 ± 2.5	-1.3 ± 2.9	-0.5 ± 2.1	0.08
SAQLI				
Domain A	0.1 ± 0.8	0.1 ± 1.7	0.2 ± 1.0	0.97
Domain B	0.1 ± 0.7	0.1 ± 1.5	0.03 ± 1.1	0.94
Domain C	0.2 ± 0.6	0.1 ± 1.2	0.2 ± 0.7	0.89
Domain D	1.0 ± 1.4	0.8 ± 1.4	1.5 ± 1.7	0.26
Domain E	–	–	–	–
Total	-0.1 ± 0.9	-0.1 ± 1.3	0.1 ± 1.0	0.73

[a]Mean ± SD. APAP, auto-adjusting positive airway pressure; ESS, Epworth Sleepiness Scale; PSQI, Pittsburgh Sleep Quality Index; SAQLI, Calgary Sleep Apnea Quality of Life Index.

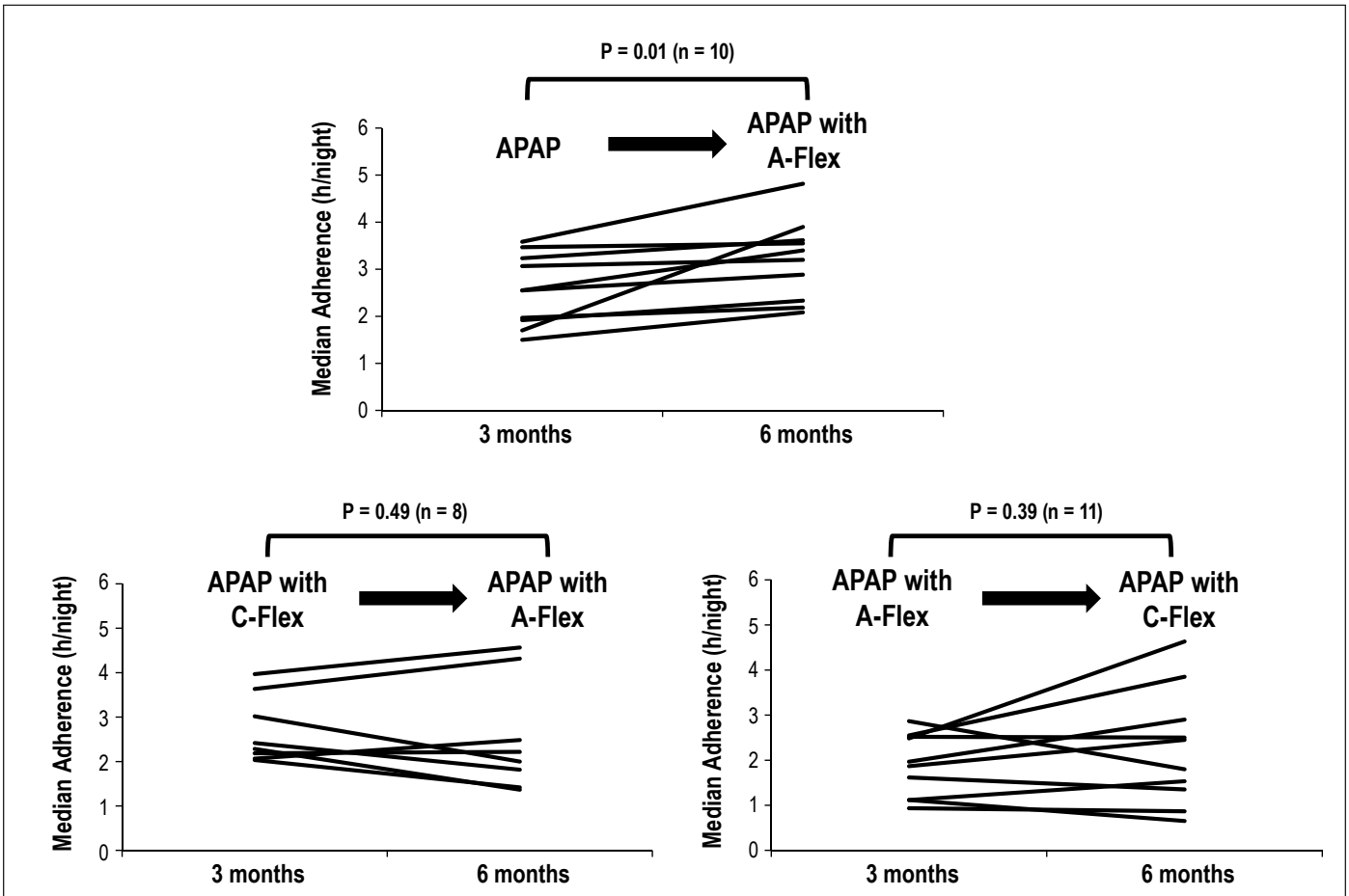

Figure 4—Analysis of poor compliers (< 4 h/night of CPAP use) between 3 and 6 mo. Individual data are presented.

C-Flex. CPAP adherence within the first 3 mo has been described as a strong predictor of long-term CPAP use.[21]

CPAP adherence is a key issue in OSA, as greater improvements in daytime sleepiness, blood pressure, and QOL occur with greater CPAP use.[22-25] A number of different variables independent of the CPAP mode can influence CPAP adherence. Older age, the use of lipid-lowering medications, the use of sedative/hypnotic agents on CPAP titration, a higher AHI, and greater daytime sleepiness were all factors shown to increase CPAP adherence.[21,26-30] In contrast, a lower body mass index (BMI) ($\leq$ 30 kg/m^2) and psychosocial factors such as living alone have been shown to be associated with poor CPAP adherence.[31,32] In the current study, there was no significant difference in these variables among the three groups. Also, all study patients received the same education on CPAP treatment. In addition, no humidification was used in any participant and their interfaces for CPAP treatment did not change during the study period. Therefore, we think that the CPAP mode was the main driver of the results of our study.

Pépin et al.[10] reported that after changing the CPAP mode from a fixed PAP to C-Flex, CPAP adherence was significantly improved in patients with low adherence (< 4 h/night of CPAP use) during the initial 3 mo, whereas this improvement did not occur in patients who were already using CPAP for > 4 h/night. These results suggest that C-Flex is an effective modality for improving adherence. Compared with patients in previous reports,[8-11] our patients had relatively low CPAP adherence (mean ± SD: 4.5 ± 1.9 h/night). Several reasons could account for this finding. As described previously, our study population had a low BMI (27.1 ± 4.7) and mild to moderate daytime sleepiness (mean ESS:,9.2 ± 4.4). It has already been described that a lower BMI and less daytime sleepiness were associated with poor CPAP adherence.[21,31] In addition, poor sleep quality and QOL were only minimally abnormal in our patients compared with previous reports.[20,32,33] Improving sleep-related QOL after CPAP in patients already having comparatively high sleep quality and QOL would seem to be difficult. Wells et al.[34] demonstrated that patients who experienced greater improvements in daily functioning had higher levels of CPAP adherence. Therefore, the absence of improvement in subjective symptoms makes it unlikely that high levels of CPAP adherence would be achieved. Taken together, our patients had several traits that could be associated with poor CPAP compliance. This might explain why C-Flex had a significant effect on CPAP adherence in the current study.

We also demonstrated that the use of APAP with A-Flex significantly improved some QOL factors and that CPAP adherence in the APAP with A-Flex group was not greater than in the APAP group. On the other hand, a significant improvement in CPAP adherence was observed in the subgroup of poor compliers who were moved from APAP to APAP with A-Flex. This result suggests that A-Flex may be an alternative CPAP mode for improving adherence in patients with poor compliance. However, further studies using randomized prospective designs are needed to confirm this result. In addition, a future study that investigates the change in PAP adherence after a switch from APAP to APAP with C-Flex is warranted.

This study had some limitations. First, our study population was Asian, and their BMI was comparatively low. Therefore, it might be difficult to apply the results of the current study to all patients with OSA. Second, this was not a double-blind but a single-blind (patients blinded) randomized study. The investigators might be influenced in their assessments by knowing the treatment received. However, the same education on PAP therapy and follow-up methods after randomization were conducted for all patients. Thus, we think this possible limitation had a minimal effect on the study outcomes.

In conclusion, this prospective, randomized study demonstrated that APAP with C-Flex led to significantly greater adherence than APAP. APAP with C-Flex is a potentially superior CPAP mode among the three tested. Although we did not observe significant changes in PAP adherence after the switch from APAP to APAP with C-Flex, A-Flex seemed to be an effective CPAP approach in patients with poor adherence to APAP.

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DISCLOSURE STATEMENT

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