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Effects of continuous positive airway pressure on blood pressure in obstructive sleep apnea patients: The Apnea Positive Pressure Long-term Efficacy Study (APPLES).

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Summary:

Obstructive sleep apnea is associated with hypertension, and short-term studies have demonstrated a modest reduction in blood pressure with continuous positive airway pressure (CPAP) therapy. We evaluated the effects of CPAP versus sham CPAP on blood pressure in 1101 participants with obstructive sleep apnea from the Apnea Positive Pressure Long-term Efficacy Study, a randomized, sham-controlled double-blinded study designed to assess the impact of CPAP on neurocognition. Participants with AHI ≥10 were randomly assigned to CPAP or sham CPAP. Blood pressures measured in morning and evening at baseline, 2 months, and 6 months were analyzed posthoc using a mixed model repeated measures analysis of variance. The largest magnitude reduction was approximately 2.4 mm Hg in morning systolic pressure that occurred at 2 months in the CPAP arm as compared to an approximate 0.5 mm Hg reduction in the sham group (CPAP effect −1.9 mm Hg, p=0.008). At 6 months, the difference between groups was diminished and no longer statistically significant (CPAP effect −0.9 mm Hg, p=0.12). Sensitivity analysis with use of multiple imputation approaches to account for missing data did not change the results. Treatment with CPAP for OSA reduces morning but not evening blood pressure in a population with well controlled blood pressure. The effect was greater after 2 than after 6 months of treatment.

Keywords

obstructive sleep apnea; hypertension; CPAP; blood pressure

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Introduction:

Obstructive sleep apnea (OSA) is highly prevalent among patients with hypertension and has been associated with increasing the risk of incident hypertension (Martínez-García et al., 2013; Muxfeldt et al., 2015; Peppard, Young, Palta, & Skatrud, 2000). OSA is characterized by repetitive closure of the upper airway resulting in apneas (complete airflow cessation) and hypopneas (partial reduction in airflow coupled with an arousal from sleep or a reduction in oxygen saturation). The resulting hypoxemia and arousals from sleep lead to increased sympathetic nervous system activity and increased chemoreflex and reduced baroreflex activity, with consequent transient elevations in nocturnal blood pressure (BP) that, like increased sympathetic activity, often persists during the day (Javaheri et al., 2017; Peppard et al., 2000). A number of randomized controlled trials have addressed the effect of OSA treatment with continuous positive airway pressure (CPAP) on resistant hypertension and have generally demonstrated a modest reduction in mean arterial pressure (Liu, Cao, Guo, & Dai, 2016; Martínez-García et al., 2013; Muxfeldt et al., 2015; Peppard et al., 2000). Data on the effects of CPAP among those without resistant hypertension is slightly more conflicting and limited (Feldstein, 2016), however, with generally short-term follow-up in sham-controlled studies. Studies with longer-term follow-up have generally been uncontrolled observational studies with smaller numbers of participants(Campos-Rodriguez et al., 2007; Sapiña-Beltrán et al., 2018). We sought to extend the literature by addressing the effect of CPAP on BP at two and six months in a posthoc analysis of data from the Apnea Positive Pressure Long-term Efficacy Study (APPLES), a randomized double blind clinical trial originally designed to assess the impact of CPAP on neurocognition. The greater duration of follow up in the APPLES study would provide more long-term data on the effects of CPAP on blood pressure in a larger sample. We hypothesized that use of CPAP would result in a sustained reduction in mean arterial BP over the 6 month duration of the study. We also hypothesized that the impact would be greater in those on fewer BP-lowering medications.(Campos-Rodriguez et al., 2007)

Methods

Study Design and Population

APPLES was a randomized, double-blinded, sham-controlled multi-center trial designed to assess the neurocognitive effects of CPAP therapy on patients with OSA. Details of the study design have previously been published (Kushida et al., 2006). Briefly, individuals aged 18–83 years old were recruited between November 2003 and August 2008 from five sleep clinics in the United States: Stanford University, Stanford, CA; University of Arizona, Tucson, AZ; Providence St. Mary Medical Center, Walla Walla, WA; St. Luke's Hospital, Chesterfield, MO; and Brigham and Women's Hospital, Boston, MA. IRB approval was obtained at all five sites, and informed consent was obtained from all participants. Those who met inclusion criteria during the initial interview underwent a diagnostic polysomnogram (PSG) at a baseline visit, and individuals with AHI ≥10/h and without severe oxygen desaturation (defined as oxygen saturation less than 75% for over 10% of the recording) were randomized to either active or sham CPAP (REMStar Pro, Phillips Respironics, Inc). Participants then underwent a sham or active titration study to determine

optimal PAP pressure and had repeat PSG and BP measurements 2 and 6 months later. We restricted the sample for the current analysis to 1,101 APPLES participants who had an AHI ≥10 after initial PSG, were initially randomized to CPAP or sham CPAP, and had an initial measurement of BP at their baseline visit.

Measures:

Polysomnography and Continuous Positive Airway Pressure—At each study time point, participants underwent a single night, 15-channel PSG. The following channels were recorded: electroencephalogram, electrooculogram, electrocardiogram, chin electromyogram, pulse oximetry, chest and abdominal excursion by inductance plethysmography, airflow by thermal sensor and nasal pressure, leg electromyography and body position. The PSG's were scored centrally using American Academy of Sleep Medicine Task Force (1999) criteria ("Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force," 1999) for sleep staging. An apnea was defined by a decrease of > 90% from baseline in the amplitude of the nasal pressure signal lasting ≥10 sec. Hypopneas were identified if there was a clear decrease (> 50% but ≤90%) from baseline in the amplitude of the nasal pressure signal, or if there was a clear amplitude reduction of the nasal pressure signal that did not reach the above criterion but it was associated with either an oxygen desaturation > 3% or an arousal, and the event duration was ≥10 seconds. The apnea-hypopnea index (AHI) was calculated as the sum of all apnea and hypopnea events divided by the hours of total sleep time (TST) (Quan et al., 2011). For participants randomized to CPAP, the optimal pressure was titrated on an overnight study. A sham titration was performed on those participants randomized to sham CPAP. A REMstar Pro CPAP system with heated humidification, mask and tubing was provided to each participant randomized to CPAP. An identical appearing unit modified to provide a trivial amount of pressure was given to participants assigned to sham CPAP. CPAP or sham CPAP adherence was monitored with a Respironics® Encore® Pro SmartCard®.

Blood Pressure

Blood pressure measurement was adapted from the Sleep Heart Health Study protocol (O'Connor et al., 2009; Quan et al., 2011) and was used by technicians trained and certified to measure resting blood pressure at all five sites. After resting for five minutes, BP was measured manually in the right arm, in triplicate, using a conventional mercury sphygmomanometer, and the average of the second and third consecutive measurements was utilized in this report. BP was measured in the evening prior to the hookup of the PSG electrodes for the diagnostic study and the morning following the diagnostic PSG at baseline as well as at the subsequent sleep studies at the two and six month follow up visits.

Statistical Analysis

Participant characteristics at baseline were compared using Student's unpaired test for continuous variables and chi squared tests for categorical variables. Blood pressures (systolic, diastolic, and mean arterial pressure [MAP]) at baseline and at the 2 and 6 month time points were analyzed posthoc using a mixed model repeated measures analysis of

variance with participants stratified by their randomization group (CPAP or Sham CPAP). Initial analyses included all eligible participants. In secondary analysis, we additionally stratified by the following *a priori* defined subgroup: participants taking or not taking antihypertensive medication. Sensitivity analyses were done using multiple imputation to assess the impact of missing data. Correlations between CPAP adherence and BP and interaction terms between treatment and adherence were tested to address impact of adherence between sham and active treatment. An interaction term between use of anti-hypertensive medications and CPAP treatment were also tested to address the impact of BP medication use between sham and active treatment on BP levels. Additionally, because body mass index (BMI, kg/m^2) increased slightly from baseline with PAP treatment, correlations between BMI and BP were also analyzed. Data are expressed as mean ± standard error (SE) or percentages. $P < 0.05$ was considered statistically significant. Analyses were performed using IBM SPSS Statistics Version 24 (Chicago, IL).

Results:

Participants on average were middle-aged, obese (mean BMI approximately 32 kg/m^2 in both arms), and had severe OSA. Baseline characteristics were similar across groups (Table 1) with no statistically significant differences across arms with the exception of PAP adherence. One third of the sample (n=371) used anti-hypertensive medication. There was a significant difference in adherence between active and sham CPAP, with 39.4% in the active treatment arm versus 21.8% in the sham CPAP arm using the treatment ≥4 hours/night for at least 70% of nights ($p < 0.001$) after 6 months. Mean hours of adherence at 2 months was 3.8±2.1 hours in the sham arm (N=394) and 4.8±2.0 in the active treatment arm (N=421, $P < 0.001$) and 3.5±2.2 hours in sham (N=347) versus 4.7±2.1 hours in the active treatment arm at 6 months (N=383, $p<0.001$).

Mean systolic and diastolic BP and MAP values at baseline, two, and six months are presented in Tables 2 (morning measures) and 3 (evening measures). At baseline, MAP was approximately 94 mm Hg in both groups in the morning and evening. There were statistically significant within-group reductions in both systolic and diastolic BP as well as in MAP in both arms at 2 and 6 months, although the magnitude of reduction was larger in the treatment arm and particularly in the morning (2.4 mm Hg reduction in morning systolic BP in the CPAP arm versus 0.5 mm Hg in sham arm, p=0.008). Active CPAP was associated with a 1.6 mm Hg greater reduction in morning MAP compared with sham CPAP after 2 months (p=0.003). By 6 months this effect was somewhat attenuated (0.9 mm Hg greater reduction in the CPAP arm, p=0.12). There were no statistically significant differences between groups in evening BP at either time point. There was no significant correlation between CPAP adherence and BP, and inclusion of a treatment*adherence interaction term did not demonstrate any impact of adherence (as a continuous measure) on the BP difference between sham and active CPAP (results not shown). Mean BMI increased by 0.13 kg/m^2 in the active CPAP group and decreased by 0.23 kg/m^2 in the sham group after 6 months ($p <0.001$); however, there was no correlation between change in BMI and BP at 6 months. 21% of participants had a missing value for morning or evening blood pressure readings at the two month visit, and 24% had a missing value for morning or evening blood pressure

readings at the 6 month visit. Sensitivity analyses using multiple imputation approaches to assess the effect of missing data found no appreciable changes in the results.

In secondary analyses, stratification by use of anti-hypertensive medication demonstrated that morning systolic, diastolic and mean BP were lower at 2 months with active CPAP compared with sham CPAP in those who were not using anti-hypertensive medications. The difference between active and sham CPAP at 2 months was −1.8 mm Hg for SBP, −1.5 mm Hg for DBP, and −1.6 mm Hg for MAP (p=0.02, 0.04, and 0.01, respectively, Table 4). This difference was attenuated and not statistically significant at 6 months. There were no statistically significant differences between groups in evening BP at 2 or 6 months (data not shown). Although CPAP appeared to produce a greater decrease in BP than sham CPAP at 2 and 6 months among those using anti-hypertensive medications, these were not statistically significant (Table 5). Testing for an interaction failed to demonstrate effect modification by anti-hypertensive medication use on BP difference between CPAP and sham CPAP. No significant changes in evening BP with either CPAP or sham CPAP were noted in those using anti-hypertensive medications (data not shown).

Discussion:

In this cohort of 1105 participants with previously undiagnosed OSA, we demonstrated a significant reduction in morning BP values at 2 months among CPAP users despite exclusion of patients with severe hypoxia who would theoretically derive the most benefit from CPAP therapy, and despite a sample with generally well-controlled blood pressure. However, the effects were slightly reduced and no longer statistically significant at 6 months among CPAP users compared to sham CPAP. The improvement in BP in the treatment arm is arguably still clinically significant, however, and suggests that CPAP use may lower BP slightly even among normotensive people or those with well-controlled BP.

Overall, this reduction in BP is less than half that seen in studies of resistant hypertension (Feldstein, 2016; Iftikhar et al., 2014; Pedrosa et al., 2013) and also somewhat lower than the 2.3 mm Hg reported at 6 weeks in a Spanish multi-center study of patients with newly diagnosed and untreated hypertension, (Durán-Cantolla et al., 2010) and the 2.4 mm Hg reported at 12 weeks from a U.S. multi-center study in patients who had generally well-controlled hypertension (Gottlieb et al., 2014). The reduction in BP is also somewhat lower than those of other smaller long-term trials assessing the effect of CPAP on BP. In the trials with the most significant improvements in BP, patients had incompletely controlled hypertension(Campos-Rodriguez et al., 2007; Huang et al., 2015) or much higher rates of adherence to CPAP(Barbé et al., 2010). The smaller BP reduction in this trial compared to prior randomized controlled studies may be explained by the use of daytime rather than nocturnal BP measurements, and by the inclusion of participants who had generally well-controlled BP or were not hypertensive, and by inclusion of participants recruited through advertisements to the general community. Such participants are less likely to have symptomatic OSA than patients recruited from sleep clinics, and there is accumulating evidence that the effect of OSA on BP and cardiovascular disease risk is greatest in symptomatic patients (Goldstein, Ancoli-Israel, & Shapiro, 2004; Kapur, Resnick, Gottlieb, & Sleep Heart Health Study Group, 2008)(Barbé et al., 2010; Craig et al., 2012; Mazzotti et

al., 2019). Although adherence to CPAP in our study was suboptimal (mean CPAP adherence 4.7 hours/night and 39.4% of participants using CPAP for ≥4 hours on at least 70% of nights) the reductions in BP we observed with CPAP are similar to the findings from a 12 month study where the mean reduction in systolic BP was 1.4 mm Hg for comparable levels of adherence (3.6 to 5.6 hours).(Barbé et al., 2010) Other trials that showed no long term reductions in blood pressure generally had worse CPAP adherence(Craig et al., 2012; McEvoy et al., 2016), were underpowered, or studied asymptomatic patients(Barbé et al., 2012). (Iftikhar et al., 2014)

Although the BP reduction in this study is modest compared with the known effect of anti-hypertensive medications, it was observed in patients whose BP generally would not be an indication for antihypertensive therapy. Moreover, the effect of CPAP treatment on BP is generally greater at night than during the day, as demonstrated in studies using 24-hour ambulatory BP monitoring (Durán-Cantolla et al., 2010), resulting in a reduction in the prevalence of nocturnal BP non-dipping (Gottlieb et al., 2014; Sapiña-Beltrán et al., 2018). As nocturnal BP with or without non-dipping is predictive of major adverse cardiovascular events independent of daytime blood pressure (Kabutoya et al., 2010; Kotruchin, Hoshide, & Kario, 2018), the modest effect observed for awake daytime BP may underestimate the cardiovascular benefit of treatment. The greater impact of CPAP on nocturnal BP likely reflects a reduction in the excess sympathetic activity that results from apnea-induced intermittent hypoxemia and recurrent arousal during the night (Javaheri et al., 2017). Carryover of this effect is the likely explanation for the greater impact of CPAP on morning BP, measured shortly after awakening, than on evening blood pressure.

Although there appeared to be a reduction in BP with CPAP in comparison to sham CPAP irrespective of the use of antihypertensive medications, it was only statistically significant in those not using anti-hypertensive medications. Nevertheless, in conjunction with inability to demonstrate a statistical interaction, it is likely that there was no effect modification by anti-hypertensive medication use in the present study. This finding contrasts with studies demonstrating a stronger effect of CPAP treatment in individuals with resistant hypertension, and with the improvements noted in past studies of treated hypertensive patients. The explanation for this finding may reflect that those on anti-hypertensive medications had very well-controlled BP leaving less room for improvement. Additionally, a smaller sample size with greater variability may have been contributing factors. Nevertheless, the data suggest that in the absence of anti-hypertensive therapy, CPAP alone can lead to a modest reduction in BP, consistent with prior studies (Durán-Cantolla et al., 2010).

As noted in some previous studies (Feldstein, 2016), a reduction in BP was also observed among participants randomized to sham CPAP. As elevated BP was not a study entry criterion, regression to the mean is not a likely explanation. A potential explanation is the Hawthorne Effect, whereby health outcomes often improve in an untreated control group due to behavior changes that result simply from the knowledge that one is being observed, such as greater medication adherence or improved diet or exercise, factors that were not measured longitudinally in this study. It is also possible that changes were made in BP medications during the course of the study in response to the closer monitoring of BP that occurred as a result of study participation. Finally, there might have been a small benefit

from the low positive pressure delivered by the sham CPAP, although prior studies using a similar sham CPAP device found no impact on OSA severity (Farré et al., 1999). Irrespective of the mechanisms responsible for producing a BP decline with sham CPAP, this observation emphasizes the importance of including a meaningful control group in future interventional studies of OSA.

To our knowledge, this is the largest randomized controlled trial in the United States to assess the effect of CPAP therapy on BP using sham CPAP for 6 months. The duration of follow-up sheds potentially important light on the effect of CPAP on BP, as the effect on mean arterial pressure diminished between 2 and 6 months from a mean of −1.6 mm Hg to a mean of −0.9 mm Hg. A similar diminution in effect of CPAP on mean arterial pressure between 6 and 12 weeks, from −2.3 to −1.5 mm Hg, was observed in a Spanish multi-center study (Durán-Cantolla et al., 2010; Farré et al., 1999). Our results are not explained by a reduction in CPAP adherence during the interim. It may reflect in part the modest weight gain seen in CPAP-treated patients, changes in antihypertensive therapy over time in response to the higher BP in sham-treated participants, or chance variation in the data; however, the possibility of diminishing effect of CPAP on BP over time should be considered in future studies. It should be noted that CPAP use lowered BP despite levels of adherence among 60% of patients that are below the criteria established by Medicare and many private insurance companies for coverage of CPAP therapy, and despite the fact that patients had well-controlled blood pressures at baseline. Although this study was not designed to determine a threshold for effective adherence, considered together with prior studies of CPAP effect on BP that achieved similar levels of adherence (Gottlieb et al., 2014), and data indicating improvements in sleepiness with levels of adherence <4 hours per night (Weaver & Grunstein, 2008)(Budhiraja et al., 2017) it calls into question the current threshold of 4 hours used to restrict CPAP reimbursement.

There are several limitations to this study. Data on medication use were not collected beyond the baseline examination, and it is therefore unknown what or how much change in anti-hypertensive medication use occurred between baseline and follow-up, which could be one explanation for the improvement in BP in the sham CPAP group. Data on diet, activity and adherence to medication were similarly not available. The study did not use 24-hour ambulatory BP monitoring, which might have produced a more accurate BP profile. There was an overall low level of adherence in the study, with only 39.4% of CPAP participants with ≥4 hours usage for more than 70% of nights. It is possible that improvement in adherence would yield a larger magnitude effect in the treatment arm, despite the lack of correlation between changes in BP and hours of adherence. Individuals with severe hypoxia were also excluded from the study, potentially excluding those most likely to benefit from treatment. Because the study included predominantly normotensive or controlled hypertensive individuals, potential for additional BP reduction by CPAP treatment was more limited. Despite the aforementioned limitations, strengths of this report include a large sample size, a randomized controlled double-blinded study design with use of a sham control arm, and use of standardized, objective PSG and BP measurement, factors that should have reduced measurement error and reporting bias and increased precision.

Conclusions:

Treatment of obstructive sleep apnea with CPAP results in significant reductions in BP at 2 months as compared to sham CPAP. At 6 months there was still a clinically significant reduction in BP in the active treatment arm, but this reduction was no longer statistically significant compared to the sham arm. This finding was present despite relatively low levels of CPAP adherence and a study population with very well-controlled BP and provides additional evidence that CPAP in persons with OSA can result in modest BP reductions.

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Table 1.

Baseline Sample Characteristics by Treatment Arm:

Variable	Sham N=547	CPAP N=558	P-value
Age	50.9 ± 0.5	52.2 ± 0.5	0.9
Male	65.6	65.2	0.9
Race			0.4
White	75.9	76.5	
Black	8.6	9.9	
Other	15.5	13.6	
Body mass index, kg/m^2	32.1 ± 0.3	32.3 ± 0.3	0.6
Alcohol servings/week	2.9 ± 0.2	3.2 ± 0.2	0.9
Current smoker	13.6	12.1	0.5
Caffeine servings/week	17.0 ± 0.6	17.4 ± 0.7	0.2
AHI	40.1 ± 1.1	39.6 ± 1.1	0.7
% SWS sleep	3.1 ± 0.2	2.9 ± 0.2	0.4
Arousal index, events/hour	30.1 ± 0.9	28.8 ± 0.8	0.3
Sleep efficiency, %	78.3 ± 0.5	78.1 ± 0.6	0.1
% Sleep time with SaO_2 <85%	2.4 ± 0.3	2.1 ± 0.3	0.4
Sleep duration, minutes	377.8 ± 2.7	375.1 ± 2.8	0.4
Hypertension	29.3	31.2	0.4
Diabetes	7.3	6.3	0.5
Coronary Artery Disease	2.0	2.2	0.9
Heart Failure	0.4	0.2	0.5
Stroke	0.6	0.6	0.5
BP medication use (yes/no)	33.1	34.1	0.7
BP medication use			0.6
ACEi or ARB	28.7	31.3	
Beta-adrenergic blocker	13.1	15.3	
Alpha-adrenergic blocker	15.6	13.4	
Diuretic Calcium-channel blocker	5.2	4.9	

Values are presented as mean ± standard error or percent

CPAP, continuous positive airway pressure; AHI, apnea hypopnea index; SWS, slow wave sleep; BP, blood pressure; ACEi, angiotensin converting enzyme inhibitor; ARB, angiotensin receptor blocker

Table 2:

Mean Morning Blood Pressure Over Time by Treatment Arm

Variable	SHAM N=544	CPAP N=555	SHAM vs. CPAP
Systolic Blood Pressure			
Baseline	124.1 ± 0.6	124.8 ± 0.6	
2 Months	123.6 ± 0.6 *	122.4 ± 0.6 *	1.9 ± 0.7 †
6 Months	122.5 ± 0.6 *	122.3 ± 0.6 *	0.9 ± 0.8
Diastolic Blood Pressure			
Baseline	79.2 ± 0.4	79.0 ± 0.4	
2 Months	78.0 ± 0.5 *	76.3 ± 0.4 *	1.5 ± 0.6 ‡
6 Months	77.9 ± 0.4 *	76.8 ± 0.4 *	0.9 ± 0.6
Mean Blood Pressure			
Baseline	94.2 ± 0.4	94.3 ± 0.4	
2 Months	93.2 ± 0.4 *	91.7 ± 0.4 *	1.6 ± 0.5 $
6 Months	92.8 ± 0.4 *	92.0 ± 0.4 *	0.9 ± 0.6

* p<0.0001 vs. Baseline for Combined Sham and CPAP

† p=0.008 vs. sham

‡ p=0.016 vs. sham

$ p=0.003 vs. sham

Table 3:

Mean Evening Blood Pressure Over Time by Treatment Arm

Variable	SHAM	CPAP	SHAM vs. CPAP
Systolic Blood Pressure			
Baseline	126.0 ± 0.5	126.2 ± 0.6	
2 Months	124.4 ± 0.6 †	124.6 ± 0.6 †	−0.2 ± 0.7
6 Months	123.8 ± 0.6 ‡	124.2 ± 0.6 ‡	0.1 ± 0.8
Diastolic Blood Pressure			
Baseline	78.6 ± 0.4	78.2 ± 0.4	
2 Months	77.9 ± 0.5 *	77.0 ± 0.4 *	−0.5± 0.6
6 Months	77.3 ± 0.5 *	77.1 ± 0.4 *	0.2± 0.7
Mean Blood Pressure			
Baseline	94.4 ± 0.3	94.2 ± 0.3	
2 Months	93.6 ± 0.3 †	92.7 ± 0.4 †	−0.7 ± 0.8
6 Months	93.0 ± 0.3 †	92.8 ± 0.3 †	0.1± 0.6

* p<0.05 vs. Baseline for Combined Sham and CPAP

† p<0.01 vs. Baseline for Combined Sham and CPAP

‡ p<0.001 vs. Baseline for Combined Sham and CPAP

Table 4:

Mean Morning Blood Pressure Over Time by Treatment Arm Among Patients Not Using Anti-hypertensive Medications

Variable	SHAM N=366	CPAP N=367	SHAM vs. CPAP
Systolic Blood Pressure			
Baseline	121.0 ± 0.6	121.1 ± 0.6	
2 Months	121.6 ± 0.6 *	119.9 ± 0.6 *	1.8 ± 0.8 ‡
6 Months	120.5 ± 0.6	119.9 ± 0.6	0.7 ± 0.9
Diastolic Blood Pressure			
Baseline	78.4 ± 0.5	77.8 ± 0.5	
2 Months	77.6 ± 0.6 †	75.6 ± 0.6 †	1.5 ± 0.7 §
6 Months	77.6 ± 0.5 †	76.3 ± 0.5 †	0.7 ± 0.7
Mean Blood Pressure			
Baseline	92.6 ± 0.5	92.2 ± 0.5	
2 Months	92.3 ± 0.5 †	90.3 ± 0.5 †	1.6 ± 0.6 ¶
6 Months	91.9 ± 0.5 †	91.0 ± 0.5 †	0.7 ± 0.7

* p<0.05 vs. Baseline for Combined Sham and CPAP

† p<0.01 vs. Baseline for Combined Sham and CPAP

‡ p=0.017 compared with sham

§ p=0.038 compared with sham

¶ p=0.01 compared with sham

Table 5:

Mean Morning Blood Pressure Over Time by Treatment Arm Among Patients Using Anti-hypertensive Medications

Variable	SHAM N=180	CPAP N=190	SHAM vs. CPAP
Systolic Blood Pressure			
Baseline	130.0 ± 1.0	131.1 ± 1.0	
2 Months	127.6 ± 1.0 *	127.3 ± 1.0 *	1.8 ± 1.2
6 Months	126.7 ± 1.0 *	126.9 ± 0.9 *	1.3 ± 1.5
Diastolic Blood Pressure			
Baseline	80.9 ± 0.5	81.3 ± 0.5	
2 Months	77.5 ± 0.8 *	77.4 ± 0.8 *	1.9 ± 1.35
6 Months	77.6 ± 0.6 *	77.7 ± 0.6 *	1.42 ± 1.1
Mean Blood Pressure			
Baseline	97.4 ± 0.7	98.2 ± 0.7	
2 Months	95.1 ± 0.8 *	94.0 ± 0.7 *	1.54 ± 1.0
6 Months	94.5 ± 0.7 *	91.0 ± 0.5 *	1.26 ± 1.1

* $p<0.001$ vs. Baseline for Combined Sham and CPAP