Systolic Blood Pressure Elevation in Children with Obstructive Sleep Apnea Is Improved with Positive Airway Pressure Use

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Introduction
To evaluate the effect of continuous positive airway pressure (CPAP) treatment on blood pressure (BP) in children with obstructive sleep apnea (OSA).

Study design
Retrospective chart review of children aged 7-17 referred to Benioff Children’s Hospital Oakland for the evaluation of snoring. Data collected included age, body mass index (BMI), BP, heart rate, apnea-hypopnea index, and oxygen saturation nadir. Children were divided into 3 groups: snorers, untreated OSA, and OSA treated with CPAP. Seventy-five children were identified, 25 in each group.

Results
There was no difference in age or apnea-hypopnea index among the groups. The CPAP group had higher BMI than the snorers and untreated OSA groups. Systolic BP was higher in the 2 OSA groups compared with the snorers. After CPAP treatment, systolic BP decreased. The BP decrease was significantly greater in patients with higher BMI at baseline. There was no significant change in diastolic BP in the 3 groups.

Conclusion
Children with OSA have higher systolic BP than habitual snorers. Treatment with CPAP in children with OSA for 6 months reduced their systolic BP despite a small increase in their BMI. (J Pediatr 2017;■■:■■–■■).

During normal sleep, the sympathetic nervous system undergoes changes that are sleep stage dependent. Non–rapid eye movement sleep is characterized by a decrease in sympathetic nervous system activity resulting in lower heart rates (HR) and blood pressure (BP). During rapid eye movement sleep, the sympathetic nervous system activity increases causing an increase in HR and BP. These physiological changes are altered in obstructive sleep apnea (OSA), leading to an increased sympathetic activation during non–rapid eye movement sleep and to dysfunction in the renin-angiotensin system, secondary to intermittent hypoxia, hypercapnia, and frequent arousals during the obstructive events.1,2 Aljadeff et al reported that children with OSA had increased sympathetic tone and decreased parasympathetic tone during sleep.3 Furthermore, Kaditis et al measured urinary catecholamines in children with various degrees of sleep disordered breathing and found that norepinephrine and epinephrine levels correlated with the obstructive apnea-hypopnea index (AHI).4 Furthermore, when compared with body mass index (BMI), age, and AHI, only age and AHI were predictors of catecholamine levels in children with OSA.5

Adult studies have shown a link between OSA and cardiovascular disease, including hypertension, arrhythmia, and ventricular dysfunction.6 OSA in children has also been associated with increased BP during the day and at night.7,9 Obese children are at higher risk of OSA and hypertension.8,10 Using 24-hour ambulatory BP monitoring, Kang et al showed that children with moderate to severe OSA had a significantly higher BP, when compared with primary snorers, independent of obesity. However, ambulatory BP monitoring has the advantage of evaluating diurnal and nocturnal changes in BP, mean BP, and BP variability.10 A comparison of ambulatory BP monitoring with single office measurements in children showed that office BP correlated well with daytime BP and night-time BP correlated better with the presence of OSA. The effect of treating OSA with continuous positive airway pressure (CPAP) on the BP in children has not been thoroughly studied.

In this study, we postulate that office measured BP levels will be higher in children with OSA when compared with habitual snorers, and that CPAP treatment will decrease BP levels in children with OSA to the levels of habitual snorers.

Methods

Our observational study consists of a retrospective chart review of children aged 7-17 years who were referred to the Benioff Children’s Hospital Oakland sleep clinic for evaluation of snoring between February 2016 and June 2017. Inclusion criteria

- AHI: Apnea-hypopnea index
- AT: Adenotonsillectomy
- BMI: Body mass index
- BP: Blood pressure
- CPAP: Continuous positive airway pressure
- HR: Heart rate
- OSA: Obstructive sleep apnea
- PSG: Polysomnography
included a completed polysomnography (PSG) and office visits: the “initial visit” was either the first consult or CPAP initia-
tion visit and a follow-up visit was done at approximately 6
months. Exclusion criteria included a known history of hy-
pertension, chronic medical conditions (pain, renal, cardiac),
medications that may alter BP (stimulants, beta blockers), and
developmental delay or syndromes.

All children had an overnight PSG per American Academy
of Sleep Medicine guidelines, using the software Sandman
Elite from Natus (Pleasanton, CA). Standard PSG leads in-
cluded 6 channels of electroencephalogram, 2 channels of
electro-oculogram, chin electromyogram, bilateral anterior
tibialis electromyogram, nasal/oral thermistor, nasal pressure
transducer, chest and abdominal wall movement belts, single
lead electrocardiogram, capnography, microphone, video moni-
toring, and pulse oximetry. The data collected were scored
by a certified sleep technologist and a board-certified sleep
physician, and included total recording time, total sleep time,
sleep efficiency (total sleep time/total recording time), sleep
latency (time from beginning of study to sleep), time spent
awake after sleep onset, arousal index (number of arousals
per hour of sleep), index of apneas and hypopneas (AHI),
time and percent in each sleep stage, index of periodic leg
movements, saturation nadir, and capnography. Obstructive
apneas were scored according to the American Academy of
Sleep Medicine Scoring of Sleep and Associated events manual
(V 2.4). An obstructive apnea was identified by a drop in
respiratory signal by 90% or more, lasting at least 2 missed
breaths and with effort evident in the chest and abdomen
belts. A hypopnea was scored when the decrease in respira-
tory signals was at least 30% lasting at least 2 breaths and
accompanied by an arousal or 3% desaturation with persis-
tent chest or abdominal effort. OSA was diagnosed according
to the International Classification of Sleep Disorders, 3rd edition,
by the presence of snoring and an AHI of at least 1. Habitual
snorers included children that snored for at least 3
nights a week, had an AHI of less than 1 on PSG, and did not
have elevated capnography on PSG (all children in this group
had normal capnography).

We performed a sample size calculation based on the
change in systolic BP obtained in the first 25 OSA subjects
treated with CPAP. If the mean difference in systolic BP between
baseline and follow-up was 8.7 with an SD of 11.4, there
would be 25 participants in the comparison groups to reject
the null hypothesis that BP difference is zero with probabil-
ty of 95% at a significance level of P < .05. For the statistical analysis, descriptive statistics were ob-
tained. Nonparametric tests were used because most variables
were found to have a non-normal (non-Gaussian) distribu-
tion. Between-group comparisons were carried out by means
of the nonparametric Kruskal–Wallis ANOVA, followed by the
Mann–Whitney test as a post hoc analysis. Within-group com-
parisons were performed using the nonparametric Wilcoxon
test for paired datasets. Correlations were assessed by means
of the linear correlation coefficient (Pearson r) and multivari-
able regression analysis. The χ² test was used for the analysis
of differences in frequencies. The significance level was set at
P < .05.

Results

Seventy-five children were included, 25 children in each group.
Fifty-seven percent of the children were male (43/75). By race/
ethnicity, 20% were white, 29% were black, 44% were His-
panic, and 7% were of another ethnic background. Only 20%
of children had undergone adenotonsillectomy (AT). The age
and ethnicity of the children in the 3 subgroups did not differ
(Table I). More males than females were in the 2 OSA groups
(P < .02; Table I). More than one-third of the children treated
with CPAP had undergone AT. AHI and oxygen saturation nadir
were not significantly different between the 2 OSA groups
(Table I). Total sleep time and sleep efficiency were reduced,
and sleep latency and wakefulness during sleep were in-
creased, in the untreated OSA group; the arousal index was
significantly higher in both OSA groups. Sleep stage distribu-
tion did not vary significantly.

The children in the treated OSA group used CPAP for 79%
of nights during the 6-month study period for an average of
6 hours per night.

The BMI, BMI z-score, systolic BP, diastolic BP, and HR at
initial and follow-up visits for the 3 groups are shown in
Table II. At the initial visit, the OSA treated group had a higher
BMI and BMI z-score than children with primary snoring
(P < .003). At follow-up, the BMI and BMI z-score in the OSA-
treated group were higher than in the untreated group and the
snorers (Table II and Figure 1). HR differences between groups
did not achieve statistical significance. In the CPAP group, the
HR decreased at follow-up (Figure 1). At baseline, the sys-
tolic BP was higher in the 2 OSA groups than the snorers. With
treatment, the systolic BP decreased significantly by 5 units,
so that it no longer was higher than that of the snorers. The
systolic BP of the untreated OSA group did not change (Table II
and Figure 1).

The relationship between the systolic BP and BMI in chil-
dren treated with CPAP is analyzed further in Figure 2. There
was no correlation between the BMI at baseline and at follow-
up. However, greater decreases in systolic BP were observed
in children who had a higher BMI at baseline (Figure 2, bottom
panel). Furthermore, the correlation between the change in the
systolic BP and BMI at baseline was significant in a multiple
regression analysis, while controlling for age, AHI, and mean
daily use of CPAP (Table III; available at www.jpeds.com).
Our data support early diagnosis and treatment of children with OSA to prevent early BP elevation.

HR also decreased in the CPAP group. Early studies have shown a correlation between HR elevation and sympathetic tone. Studies in adults have shown an association between HR and hypertension in patients with OSA, with the mean HR correlating with the AH1. Furthermore, studies have shown that an increased HR at diagnosis predicts a more significant CPAP effect on BP measurements. Although our CPAP group did not show a significant increase in HR at the initial visit, a decrease in HR at the follow-up visit points to the beneficial 22,21

Table I. Demographic and clinical features of the subjects

<table>
<thead>
<tr>
<th></th>
<th>Snorers (n = 25)</th>
<th>Untreated OSA (n = 25)</th>
<th>OSA treated with CPAP (n = 25)</th>
<th>Kruskal-Wallis ANOVA</th>
<th>Mann-Whitney test</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (y), median (25-75 percentile)</td>
<td>12 (11-13)</td>
<td>14 (12-16)</td>
<td>13 (10-15)</td>
<td>3.824</td>
<td>NS</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>9</td>
<td>15</td>
<td>19</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>16</td>
<td>10</td>
<td>6</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Race</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>4</td>
<td>7</td>
<td>4</td>
<td></td>
<td></td>
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<tr>
<td>Black</td>
<td>6</td>
<td>8</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hispanic</td>
<td>14</td>
<td>8</td>
<td>11</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>2</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI, z-score, median (25-75 percentile)</td>
<td>1.9 (1.2-2.3)</td>
<td>2.4 (1.9-2.5)</td>
<td>2.6 (2.0-2.8)</td>
<td>12.679</td>
<td>.0018</td>
</tr>
<tr>
<td>AT, yes/no (unknown)</td>
<td>4/20 (1)</td>
<td>2/23 (0)</td>
<td>9/16 (0)</td>
<td>6.35*</td>
<td>.042</td>
</tr>
<tr>
<td>AHI, median (25-75 percentile)</td>
<td>0.5 (0.3-0.8)</td>
<td>7.7 (4.3-22)</td>
<td>13.0 (8.8-19)</td>
<td>50.415</td>
<td>.0001</td>
</tr>
<tr>
<td>Oxygen saturation nadir, median (25-75 percentile)</td>
<td>93 (90-94)</td>
<td>89 (83-92)</td>
<td>89 (81-90)</td>
<td>21.489</td>
<td>.0001</td>
</tr>
<tr>
<td>Total sleep time (min), median (25-75 percentile)</td>
<td>410 (372-426)</td>
<td>369 (361-389)</td>
<td>402 (367-423)</td>
<td>8.358</td>
<td>.006</td>
</tr>
<tr>
<td>Sleep latency (min), median (25-75 percentile)</td>
<td>15 (8-25)</td>
<td>34 (23-44)</td>
<td>10 (4-25)</td>
<td>10.359</td>
<td>.0017</td>
</tr>
<tr>
<td>Sleep efficiency (%), median (25-75 percentile)</td>
<td>15 (10-15)</td>
<td>13 (7-18)</td>
<td>15 (7-18)</td>
<td>2.748</td>
<td>NS</td>
</tr>
<tr>
<td>WASO (min), median (25-75 percentile)</td>
<td>50 (22-75)</td>
<td>78 (22-113)</td>
<td>41 (17-61)</td>
<td>6.076</td>
<td>NS</td>
</tr>
<tr>
<td>Periodic leg movements index (number), median (25-75 percentile)</td>
<td>5 (4-6)</td>
<td>7 (6-11)</td>
<td>9 (6-15)</td>
<td>17.366</td>
<td>NS</td>
</tr>
</tbody>
</table>

Table II. Between-group comparisons of BMI, systolic BP, diastolic BP, and HR at diagnosis (or CPAP initiation) and 6 month follow-up

<table>
<thead>
<tr>
<th></th>
<th>Snorers Median (25/75 centile)</th>
<th>Untreated OSA Median (25/75 centile)</th>
<th>OSA treated with CPAP Median (25/75 centile)</th>
<th>Kruskal-Wallis ANOVA</th>
<th>Mann-Whitney test</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI, baseline</td>
<td>24.8 (21.6/31.6)</td>
<td>31.7 (25.5/38.8)</td>
<td>37.7 (28.7/46.2)</td>
<td>9.767</td>
<td>.0076</td>
</tr>
<tr>
<td>BMI, follow-up</td>
<td>25.3 (22/32.6)</td>
<td>32.9 (25.9/37)</td>
<td>40.1 (30.4/46.6)</td>
<td>9.879</td>
<td>.0072</td>
</tr>
<tr>
<td>BMI, baseline</td>
<td>0.5 (0.5-1.9)</td>
<td>0 (0-9.1)</td>
<td>1.3 (0.22)</td>
<td>5.147</td>
<td>NS</td>
</tr>
<tr>
<td>BMI, follow-up</td>
<td>1.9 (1.4-2.3)</td>
<td>2.4 (1.9-2.5)</td>
<td>2.6 (2.0-2.8)</td>
<td>12.679</td>
<td>.0018</td>
</tr>
<tr>
<td>BMI, baseline</td>
<td>0.06 (0.00-0.05)</td>
<td>0.00 (0-0.00)</td>
<td>0.05 (0.00-0.09)</td>
<td>9.080</td>
<td>.011</td>
</tr>
<tr>
<td>HR, baseline</td>
<td>77 (73/93)</td>
<td>86 (80/100)</td>
<td>87 (84/103)</td>
<td>5.760</td>
<td>NS</td>
</tr>
<tr>
<td>HR, follow-up</td>
<td>83 (76/91)</td>
<td>89 (77/99)</td>
<td>83 (77/95)</td>
<td>1.412</td>
<td>NS</td>
</tr>
<tr>
<td>HR, delta</td>
<td>1 (1-12.9)</td>
<td>0 (0-12.9)</td>
<td>0 (0-12.9)</td>
<td>2.552</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic BP, baseline</td>
<td>112 (105/114)</td>
<td>116 (113/122)</td>
<td>118 (112/131)</td>
<td>10.847</td>
<td>.0034</td>
</tr>
<tr>
<td>Systolic BP, follow-up</td>
<td>112 (105/115)</td>
<td>121 (115/128)</td>
<td>112 (106/122)</td>
<td>10.497</td>
<td>.0053</td>
</tr>
<tr>
<td>Systolic BP, baseline</td>
<td>–1 (–7/6)</td>
<td>4 (0/10)</td>
<td>–5 (–19/0)</td>
<td>15.131</td>
<td>.005</td>
</tr>
<tr>
<td>Systolic BP, follow-up</td>
<td>–1 (–7/6)</td>
<td>4 (0/10)</td>
<td>–5 (–19/0)</td>
<td>15.131</td>
<td>.005</td>
</tr>
<tr>
<td>Diastolic BP, baseline</td>
<td>67 (60/69)</td>
<td>68 (64/71)</td>
<td>67 (65/72)</td>
<td>2.639</td>
<td>NS</td>
</tr>
<tr>
<td>Diastolic BP, follow-up</td>
<td>45 (58/69)</td>
<td>70 (67/80)</td>
<td>68 (62/72)</td>
<td>7.118</td>
<td>.029</td>
</tr>
<tr>
<td>Diastolic BP, delta</td>
<td>1 (–4/4)</td>
<td>4 (0/10)</td>
<td>–1 (–6/7)</td>
<td>4.901</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.
Increased BP and hypertension are proven consequences of OSA in adults, with evidence supporting the same pattern in children. The mechanism of increased BP can be multifactorial, but activation of the sympathetic nervous system during sleep in patients with OSA is thought to be the cause of systolic hypertension. Another important contributor to increases in BP in patients with OSA is a dysfunction in the renin-angiotensin system. The levels of angiotensin II, a potent vasoconstrictor, are increased in adults with OSAS compared with controls. Diastolic BP did not increase in our patients, matching previous published data in adults with OSA. The mechanism has not been fully elucidated; although systolic hypertension is associated with intermittent hypoxia and increased sympathetic activity as seen in OSA, diastolic hypertension has been associated with increased in peripheral vascular resistance as in patients with hyperlipidemia and obesity.

Horne et al studied BP and HR in 44 school-age children with mild to severe OSA, 61 primary snorers, and 36 controls and concluded that children with sleep disordered breathing, regardless of severity, had BPs that were 10-15 mm Hg higher than controls. This increase was evident during both

**Figure 1.** A–C, Within-group comparison of BMI, systolic BP, diastolic BP, and HR at the initial visit and the follow-up visit by the Wilcoxon test for paired datasets. Data are expressed as median (small squares), interquartile range (boxes), nonoutlier range (whiskers), and outliers (small circles). Units for BP are mm Hg, for BMI weight/height$^2$, and for HR beats per minute.

**Figure 2.** Correlation between BMI at baseline and A, change of BMI at follow-up or B, change in systolic BP at follow-up in children treated with CPAP.
wakefulness and sleep. In another study of 105 elementary school-aged children with OSA, BP measured while awake and asleep was 10 to 15 mm Hg greater than 36 nonsnoring control patients.8 The 24-hour BP recordings in 96 children demonstrated that children with a higher AHI had a significantly higher systolic BP while awake, and higher systolic and diastolic BP while asleep, independent of OSA severity with significant reductions in 24-hour ambulatory BPs noted after AT.9 Other studies have corroborated this effect of AT on children with OSA and hypertension, showing a decrease in BP after AT, although some children still had hypertension.10,11 In adults, there is evidence that treatment of OSA with CPAP reduces BP.12 Contrary to the benefits of CPAP on BP, a positive effect of CPAP on BP in children with OSA has not been shown.13 Most studies on the use of CPAP in children have focused on improvements in AHI.14,15 Marcus et al showed improvement on behavior after 3 months of CPAP use. Studies on cardiovascular effects of CPAP in children are lacking.16

The limitations to our study include an observational retrospective chart review, small cohort, a single recruiting center, single BP measurement at an office visit, and lack of confirmatory cardiovascular evaluation such as echocardiogram. Ethically, we cannot randomize children to receive or withhold CPAP, so a retrospective design comparing children who did and did not receive CPAP based on clinical decisions was most practical. Despite these limitations, we report PSG for all patients and have demonstrated an effect of CPAP on BP.

In conclusion, our study demonstrates higher systolic BP in “normotensive” children with OSA when compared with controls. This systolic BP in children with OSA is decreased after 6 months of treatment with CPAP, suggesting early awareness and proper treatment of OSA in children should be advocated.

References


Table III. Results of the multiple regression analysis between change in systolic BP (dependent variable) and different independent variables (BMI at baseline, age, AHI, and mean daily use of CPAP, in the group of children treated with CPAP)

<table>
<thead>
<tr>
<th></th>
<th>Partial correlation</th>
<th>R-square</th>
<th>t(20)</th>
<th>P &lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI at baseline</td>
<td>−0.451</td>
<td>0.431</td>
<td>−2.258</td>
<td>.035</td>
</tr>
<tr>
<td>Age</td>
<td>0.165</td>
<td>0.308</td>
<td>0.749</td>
<td>NS</td>
</tr>
<tr>
<td>AHI</td>
<td>0.032</td>
<td>0.211</td>
<td>0.142</td>
<td>NS</td>
</tr>
<tr>
<td>Mean daily use</td>
<td>−0.045</td>
<td>0.296</td>
<td>−0.203</td>
<td>NS</td>
</tr>
</tbody>
</table>

NS, not significant.