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Original Article

Improvement of sleep-disordered breathing in children is associated with a reduction in overnight blood pressure

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ABSTRACT

Objective: Childhood sleep-disordered breathing (SDB) is associated with elevated blood pressure (BP); however, little is known about the long-term outcomes in this population. We aimed to assess long-term changes in overnight BP in children with SDB.

Methods: Forty children with previously diagnosed SDB and 20 nonsnoring control participants underwent repeat overnight polysomnography (PSG) with continuous BP measurement 4 years after the original diagnosis. At follow-up, children aged 11–16 years were categorized into 2 groups of resolved (absence of snoring and obstructive apnea–hypopnea index [OAHI]$\leqslant$1) or unresolved (continued to snore or had an OAHI >1) SDB.

Results: There were no group differences in age, sex, or body mass index (BMI) *z* score. OAHI was lower at follow-up ($P < .05$) in both the resolved ($n = 18$) and unresolved ($n = 22$) groups. BP was elevated during wake and sleep in both SDB groups compared to the control group at baseline ($P < .01$ for all), but it decreased by 5–15 mmHg at follow-up during sleep for both SDB groups ($P < .05$ for all). BP during wake was unchanged in the SDB groups at follow-up but increased in the control group ($P < .05$). At follow-up, BP did not differ between the control group and the SDB groups during wake or sleep. Improved oxygen saturation (SpO_2) during sleep was a significant predictor of a reduction in BP.

Conclusions: SDB improved over the 4-year follow-up and both resolved and unresolved groups exhibited a significant reduction in BP during sleep, with levels similar to the control group. Our study highlights the fact that even small improvements can improve the cardiovascular effects of SDB.

1. Introduction

The association between sleep-disordered breathing (SDB) and adverse cardiovascular outcomes in adults is widely acknowledged, and although far fewer studies exist in the pediatric population accumulating evidence strongly suggests that there also are adverse effects on the cardiovascular system in children [1]. Childhood SDB is common, with the reported prevalence dependent on the severity of the disorder. The most severe form, obstructive sleep apnea (OSA), is characterized by snoring, intermittent hypoxia, or sleep fragmentation and has been reported to occur in 1–5% of children [2]. However, a far greater proportion of children (up to 35%) [3] are affected by primary snoring (PS), which is not associated with gas exchange abnormalities or sleep disturbance. Because the most common cause of childhood SDB is the presence of large tonsils or adenoids, the first-line treatment is adenotonsillectomy (T&A).

Similar to adults, factors such as hypoxia and arousals from sleep potentially lead to inflammation, endothelial dysfunction, and sympathetic activation and have been implicated in OSA-mediated cardiovascular morbidity in children [1]. Several studies have shown that blood pressure (BP) is elevated in children with both OSA and PS [4–8]. Heart rate (HR) also has been shown to be higher in children with OSA [8]. Although there are numerous studies examining the effectiveness of T&A on the improvement or resolution of SDB, scant data are available assessing its effect on cardiovascular outcomes [9]. In adults, treatment of OSA using continuous positive airway pressure (CPAP) has been shown to modestly reduce BP levels by 1–2 mmHg [10] and reduce the incidence of hypertension [11]. Only 3 studies have assessed the effect of treatment on BP outcomes in children and the results of these have been variable, showing no change in BP [12], an increase in those with a recurrence of SDB [13], and improvements only in diastolic BP [14]. These studies were limited, as they had short follow-up times ($\leqslant$1 y) and used either office or ambulatory BP measures. Furthermore, there are no studies examining BP outcomes for

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children with milder SDB such as PS, who are not commonly treated and make up the largest proportion of children affected with SDB. Hence the aim of our study was to assess wake and continuous overnight BP and HR in both children with resolved and unresolved SDB together with nonsnoring control children over a long follow-up period (4 y). We hypothesized that overnight BP and HR in children with resolved SDB would return to levels observed in control children and remain elevated in children with unresolved SDB at 4-year follow-up.

2. Methods

Approval for our study was granted by the Southern Health and Monash University Human Research Ethics Committees. Participation was voluntary and no monetary incentive was offered. Written informed consent was obtained from parents and verbal assent was obtained from the children on the night of the study.

2.1. Participants and study design

Our study began in 2009 and we prospectively recruited children who were originally studied between July 2004 and December 2008 when they were aged 7–13 years. One hundred and fifty-five children, 116 of whom had been referred for assessment of suspected SDB, and 39 nonsnoring control children who were recruited from the community, were studied at baseline. The effect of SDB at baseline on BP [8,15], cardiovascular control [16], behavior and neurocognition [17,18], and sleep quality [19] has been previously published. Children without an adequate BP recording at baseline or those originally studied in 2004 were excluded from the follow-up study, as this study aimed to reassess BP within a 4-year timeframe, leaving 135 children (SDB [$n = 99$]; control [$n = 36$]) eligible to participate. Of these 135 children, 16 were unable to be contacted. The remaining 119 children (SDB [$n = 83$]; control [$n = 36$]) were invited to participate in our study and from those 63 (SDB [$n = 42$]; control [$n = 21$]) participated. Socioeconomic status (SES) was determined for each child according to the Australian Bureau of Statistics Socio-Economic Indexes for Areas (2006), which is based on postal code [20]. Treatment type (if any) received for SDB after initial diagnosis was documented by parental report on the night of the follow-up study. Treatment was not standardized as part of the study and reflected the clinical decision of the treating physician and the wishes of the parents.

2.2. Protocol

Anthropometric measures including height and weight were recorded and body mass index (BMI) was calculated and converted to BMI z scores [21]. All participants including the control group underwent overnight polysomnography (PSG) using a commercially available PSG system (Series S or Series E Sleep System, Compumedics, Melbourne, Australia at baseline and Series E Sleep System at follow-up). The children went to bed once lead application was completed and were awakened at 6:00 am. The following signals were recorded: electroencephalography (Cz, C4-A1, C3-A2, O2-A1, O1-A2), left and right electrooculogram, submental electromyogram (EMG), left and right anterior tibialis muscle and EMG, and electrocardiogram. Oxygen saturation (SpO_2) was measured using Masimo Radical®SET (Masimo Corp., CA, USA) at baseline and the Bitmos GmbH, (Dusseldorf, Germany) at follow-up, both of which use Masimo signal extraction technology (SET) for signal processing. All oximeters were set to a 2-s averaging time. Transcutaneous carbon dioxide was measured at baseline using a TCM4/40 (Radiometer, Copenhagen, Denmark) and at follow-up using a TINA TCM3 (Radiometer, Copenhagen, Denmark). Respiratory parameters recorded included thoracic and abdominal respiratory inductance plethysmography (Pro-Tech zRIP™ Effort Sensor, Pro-Tech Services Inc., Mukilteo, WA, USA), nasal pressure (Salter Style®, Salter Labs, Arvin, CA, USA), and oronasal airflow (Sandman®BreathSensor™, Child Airflow Thermistor, Tyco Healthcare, UK). The signal recordings that were obtained were the same as previously reported in the baseline study except for the following: (1) SpO_2 was measured using Masimo Radical®SET (Masimo Corp., CA, USA) at baseline and the Bitmos GmbH, (Dusseldorf, Germany) at follow-up, both of which use Masimo SET for signal processing; and (2) transcutaneous carbon dioxide was measured at baseline using a TCM4/40 (Radiometer, Copenhagen, Denmark) and at follow-up using a TINA TCM3 (Radiometer, Copenhagen, Denmark).

BP was continuously and noninvasively measured using finger arterial photoplethysmography with a Finometer™ (Finapres Medical Systems, Amsterdam, Netherlands). The Finometer™ records beat-to-beat BP with the ability to reconstruct brachial artery pressure waveforms and has been validated for use in adults [22,23] and infants [24]. The same Finometer™ was used to obtain BP measurements at baseline and follow-up. Wake BP was measured while the participant was lying quietly in bed prior to lights out for a minimum of 10 min. BP recording was continued throughout the night while participants were asleep. Finometer™ BP measurements were validated by comparing values with at least 3 simultaneous measurements of office BP performed with an aneroid sphygmomanometer (Big Ben Reister, Rudolf Riester, Jungingen, Germany) at baseline and Dinamap (V100, CARESCAPE™, Freiburg, Germany) at follow-up, using an appropriately sized cuff. The Dinamap device has been previously validated for assessing BP in children [25,26]. Comparisons of BP measurements were made with the participant lying supine during quiet wakefulness at the completion of PSG lead attachment. All Finometer™ measurements for systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) were within 5 mmHg of the office BP measurements. There was no difference in SAP ($P = .14$) or DAP ($P = .39$) measurements between those taken by the Finometer™ (SAP, 107.1 ± 1.1 mmHg; DAP, 58.3 ± 0.7 mmHg) and Dinamap (SAP, 105.8 ± 1 mmHg; DAP, 57.9 ± 0.6 mmHg).

2.3. Data analysis

All PSG studies were sleep staged in 30-s epochs by experienced pediatric sleep technologists, with respiratory and sleep parameters being scored and calculated using the same protocol as previously published for the baseline study [8]. Because the initial PSG studies were conducted before the implementation of the American Academy of Sleep Medicine new scoring rules [27], all PSG studies were sleep staged using Rechtschaffen and Kales criteria [28] by experienced pediatric sleep technologists into wake after sleep onset (WASO); nonrapid eye movement sleep stages 1 (NREM1), 2 (NREM2), 3 (NREM3), and 4 (NREM4); and rapid eye movement (REM) sleep. Sleep technologists were blinded to previous SDB severity or diagnostic group. Respiratory events were scored if they were $\geqslant 2$ respiratory cycles in duration, and the classification of apneas and hypopneas was based on standard criteria [29] with minor modifications in accordance to clinical practice at the time of the baseline study. Apneas and hypopneas were not scored during periods of body movement and instead were scored from the end of expiration to the beginning of inspiration. Obstructive hypopneas required a clear reduction from baseline in flow signal, continued respiratory effort present with paradox or phase shift and to be associated with snoring, or noisy breathing during or at the termination of the event. Obstructive hypopneas were either associated with an awakening, an arousal, or a $\geqslant 3\%$ oxygen desaturation. The extent of reduction in airflow was not measured and a clear reduction was all that was required. Arousals were