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Original Article

Overweight and obese children with sleep disordered breathing have elevated arterial stiffness

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ABSTRACT

Background: The prevalence of obese children with sleep disordered breathing (SDB) is increasing. Obesity and SDB are independent cardiovascular risk factors, of which arterial stiffness is an early sign. Pulse wave velocity (PWV), is a marker of arterial stiffness and central systolic blood pressure (cSBP) is a better predictor of cardiovascular outcome than peripheral blood pressure. Therefore, we aimed to determine PWV and cSBP in overweight/obese or normal weight children with sleep disordered breathing (SDB), and non-snoring normal weight controls.

Methods: Children (3-18 y) with SDB (overweight/obese [BMI z-scores $\geq$ 1.04], n = 48; normal weight n = 44) referred for clinical assessment of SDB and normal weight non-snoring controls recruited from the community (n = 38) underwent overnight polysomnography. PWV was calculated using photoplethysmography. cSBP was calculated using applanation tonometry in a subset of children older than 8 y (n = 55) who had usable waveforms.

Results: Overweight/obese SDB group had higher PWV (mean cm/s (95% CI); wake: 366 (355–380); sleep: 340 (324–357)), than the normal-weight SDB group (wake: 257 (247–267), p = 0.002; sleep: 255 (242–269), p = 0.005), and non-snoring controls (wake: 238 (226–249), p = 0.002; sleep: 235 (220–250), p < 0.001). The normal-weight SDB group had higher PWV than controls (p = 0.03). Overweight/obese children with SDB had higher cSBP (105 (100–110) mmHg) compared with the normal weight children with SDB (96 (90–102)) and the non-snoring controls (97 (91–104); p < 0.05 for both).

Conclusion: This study suggests that overweight/obesity substantially worsens the cardiovascular sequelae of SDB, highlighting the imperative to treat obesity and SDB in children early in order to reduce future cardiovascular disease risk.

1. Introduction

Sleep disordered breathing (SDB) follows a continuum of severity from primary snoring to obstructive sleep apnea (OSA), and affects up to 11% of children [1]. This means that eight million children under 17 years in the USA alone [2] are impacted by a condition associated with clinically significant deficits in neurocognitive [3], behavioral [4] and cardiovascular outcomes [5–9]. Obesity contributes significantly to this statistic as the prevalence of OSA in obese children is nearly 80% depending on the definition of OSA and obesity [10], compared to 6% in the general pediatric population [11]. OSA is characterized by repetitive respiratory events of either complete (apnea) or partial (hypopnea) obstruction to airflow, resulting in hypoxia, hypercapnia and arousal [11]. During each respiratory event there is a period of bradycardia and a concomitant fall in blood pressure (BP), followed at event termination by significant tachycardia and surge in BP [12]. It is these repetitive episodes of hypoxia, arousal, and significant fluctuations in heart rate (HR) and BP, which increase sympathetic activity and cause transient vasoconstriction, resulting in elevated BP [5–7,9]

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and cardiac remodelling [5] in children with OSA. Furthermore, even primary snoring is not benign, as children with this milder disease also exhibit elevated BP [6,9]. It is important to identify and treat the underlying causes of elevated BP as increased BP levels during childhood predict hypertension in young adults [13].

Evidence suggests that central blood pressure is more strongly related to surrogate measures of cardiovascular risk including carotid intima-media thickness and left ventricular mass than brachial blood pressure in adults [14]. Arterial tonometry provides a simple and non-invasive estimation of central aortic systolic BP (cSBP) and augmentation index (AI) from the radial artery pulse waveform [15–17]. The AI represents the augmentation of the central aortic pressure by a reflected pulse wave.

Arterial stiffness is linked to poor cardiovascular outcomes [18], however the temporal relationship between hypertension and arterial stiffness remains to be elucidated. Early childhood marks the beginning of natural age-related changes to arterial wall properties, and obese children have a higher risk of blood vessel damage and cardiovascular disease compared with their normal-weight peers [19]. Obese children without SDB exhibit increased intima-media thickness and stiffness of the carotid artery [20,21], and increased pulse wave velocity (PWV) [22]. PWV is considered the gold standard for non-invasive assessment of arterial stiffness. Increased arterial stiffness has been associated with SDB in adults [23–25]. Similar studies have not been conducted in the pediatric population. Therefore, the aim of this study was to identify if overweight/obese children with SDB (3–18 y) had increased measures of arterial stiffness (PWV and AI) and cSBP compared with normal-weight children with SDB and normal weight non-snoring controls. We hypothesized that the effects of SDB and increased BMI would be cumulative and overweight/obese children would have increased PWV, AI and cSBP compared with normal weight children with or without SDB.

2. Methods

Ethical approval for this project was granted by the Monash Health and Monash University Human Research Ethics Committees. Written informed consent was obtained from parents and verbal assent from the children after a full explanation of the procedure. There was no monetary incentive for participation.

Participants were children (aged 3–18 years) attending the sleep center for clinical assessment of suspected SDB ($n = 92$) and age-matched non-snoring children recruited from the community ($n = 38$). All children were born at term and children with conditions or taking medications known to affect sleep, breathing, or blood pressure were not recruited. Children were otherwise normal, did not have diabetes or insulin resistance, and were not undergoing treatment with either nasal steroids or antibiotics on the day of the study or for the preceding two weeks.

2.1. Protocol

All children underwent overnight attended polysomnography (PSG) in a clinical pediatric sleep centre. Height and weight were measured and converted to a body mass index (BMI) z-score to adjust for sex and age [26]. Obesity was defined as $\geq$ 95th percentile (BMI z-scores $\geq$ 1.65) and overweight as $\geq$ 85th percentile (BMI z-scores $\geq$ 1.04) as computed by using Centers for Disease Control and Prevention 2000 growth standards http://www.cdc.gov/growthcharts and software (Epi Info [Centers for Disease Control and Prevention, Atlanta, GA]). The distance from the suprasternal notch to the tip of the non-dominant ring finger was measured for pulse transit time (PTT) analysis. Prior to sleep, three wake brachial BP measurements were performed using an automated oscillometric device (CARESCAPE™ V100 Dinamap, GE Medical systems, Germany). Systolic BP (SBP) and diastolic BP (DBP) were recorded and mean BP pressure (MAP) calculated (SBP+(2xDBP))/3.

Electrophysiological signals were recorded using a commercially available PSG system (E-Series, Compumedics, Melbourne, Australia) using standard pediatric techniques [7]. In summary, electroencephalogram, left and right electrooculogram, submental electromyogram, left and right anterior tibialis muscle electromyogram and electrocardiogram (ECG) were attached. Thoracic and abdominal breathing movements, transcutaneous carbon dioxide, nasal pressure (a semi-quantitative measurement of nasal airflow), oronasal airflow and oxygen saturation (SpO2) were recorded. PSG studies were manually scored in 30 s epochs according to clinical practise [27]. Both the ECG and the PPG were sampled at 512 Hz. Following the PSG study, data were transferred via European Data Format to data analysis software (LabChart v 7.3.7, ADInstruments, Sydney, Australia) for detailed cardiovascular analysis. SDB severity was based on the OAHI, which was defined as the total number of obstructive apneas, mixed apneas, obstructive hypopneas, RERAD (respiratory event related arousal/desaturation) per hour of total sleep time. The controls differed from children with primary snoring in the clinical group, as the controls had no history of snoring and snoring was not detected on the PSG.

Children were initially grouped into Control, Normal Weight PS, Normal Weight OSA, Overweight/Obese PS, and Overweight/Obese OSA groups for analysis. Subsequently, as the number of overweight/obese children with PS was small ($n = 13$), children with PS and those with OSA were combined into normal weight and overweight/obese SDB groups. The initial analysis demonstrated that there was no statistical difference in PWV between the PS and OSA groups for either of the normal weight or overweight/obese children (data not shown). Furthermore, the appropriateness of combining the PS and OSA groups is evidenced by studies that have identified that children with PS have similar cardiovascular outcomes as children with OSA [6,9].

2.2. Pulse wave velocity (PWV)

PWV was calculated beat-to-beat and averaged into 30 s artifact-free epochs during wake (minimum 10 min before sleep onset) and sleep (the entire night excluding periods of wake), such that: PWV = Äx/PTT where Äx is the distance travelled in the artery, measured exteriorly on each child as the distance from the tip of the finger to the suprasternal notch [16,28]. Calculating PWV by photoplethysmography has been validated using correlation with intra-arterial sensing techniques [29]. PTT was calculated using our previously published method [7]. The peak of the ECG R-wave and the 50% point of the height of the corresponding pulse wave (Fig. 1), were identified by peak detection for each beat in LabChart v7.3.7. PTT was calculated as the time delay between those two points.

2.3. Central aortic systolic blood pressure (cSBP) and augmentation index (AI)

Prior to sleep and immediately following the brachial BP measurements, radial arterial pressure waveforms were acquired with a Millar Mikro-Tip tonometer (SPT-301 Non-invasive Pulse Tonometer, Miller Instruments, Texas, USA), digitized (Powerlab, ADInstruments, Sydney, Australia) and recorded onto Labchart 7 v 7.3.7 for data storage and analysis at a sampling rate of 1000 Hz. Obtaining suitable quality waveforms for analysis in young children is difficult. Therefore we conducted arterial tonometry on a