



Pollen levels on the day of polysomnography influence sleep disordered breathing severity in children with allergic rhinitis

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Received: 3 October 2018 / Revised: 14 February 2019 / Accepted: 25 February 2019 / Published online: 5 March 2019
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Abstract

Purpose Allergic rhinitis (AR) is a common risk factor for sleep disordered breathing (SDB) in children. Allergy to pollen is a trigger for allergic rhinitis, causing nasal inflammation, upper airway congestion and obstruction. We aimed to determine if the pollen count on the day of diagnostic polysomnography for SDB affected the result.

Methods Children (3–18 years; $n = 90$) who participated in research studies between 1 October and 31 December, when daily regional pollen counts were available, in the years 2005–2016 were eligible for inclusion. All children underwent overnight polysomnography for assessment of SDB severity. Pollen was categorised as grass or other pollen. Multiple stepwise linear regression was performed to determine whether the pollen count for that day, a diagnosis of asthma, age, and BMI-z-score were determinants of respiratory parameters measured on polysomnography, including the obstructive apnoea hypopnoea index (OAH), SpO_2 nadir, average SpO_2 drop, $SpO_2 < 90\%$, oxygen desaturation index $> 4\%$ (ODI4), and average transcutaneous CO_2 (TCM).

Results Sixteen/90 children had AR. In children with AR, an increase in grass pollen of 1 grain/m³ predicted an increase in OAH of 0.2 events/h, ODI4 of 0.18 times/h, $SpO_2 < 90\%$ of 0.03 times/h, and TCM of 0.07 mmHg. None of the factors were determinants of SDB severity in children without AR.

Conclusion Our findings highlight that daily pollen counts may be an important factor influencing the severity of SDB on a single night of polysomnography in children with clinical allergic rhinitis and should be taken into account when determining treatment options.

Keywords Allergy · Paediatric · Obstructive sleep apnoea · Sleep

Introduction

Sleep disordered breathing (SDB) is a common condition, affecting up to 11% of children [1]. SDB forms a continuum of severity from primary snoring to severe obstructive sleep apnoea (OSA) and is commonly associated with adenotonsillar hypertrophy. The tonsils and adenoids are the site where food and

airborne allergens often come into contact with the body's immune system for the first time. Allergic rhinitis (AR) is an immunoglobulin E-mediated response to an airborne allergen, such as pollen, in a sensitised person. AR is a common comorbidity in children with SDB [2, 3] and may contribute to nasal obstruction through nasal mucosal inflammation and/or adenoidal hypertrophy [4, 5].

Pollen from certain wind-pollinated plants is the main AR trigger in the outdoor environment. The plants which contribute most to pollen allergies in Australia are grasses [6], with a single plant able to release millions of pollen granules into the air. Pollen counts in Melbourne, Australia, are highest in the spring between October and December. The acute response to allergens, such as pollen, in children with AR is an immunoglobulin E (IgE)-mediated inflammation of the nasal mucosa, which leads to mucosal oedema and nasal congestion, causing upper airway obstruction [7, 8]. Therefore, the aim of this

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study was to determine whether the pollen count recorded on the same day as the diagnostic polysomnographic study for suspected SDB would affect SDB severity. We hypothesised that in children with AR, the pollen count would be a significant predictor of SDB severity on that day. We also hypothesised that in children without AR, pollen count would have no effect on SDB severity.

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

This was a retrospective analysis of data from children (aged 3–18 years) attending our sleep centre for clinical assessment of suspected SDB ($n = 90$) between 1 October and 31 December in the years 2005–2016. These months coincide with spring and early summer, the only months when daily pollen counts were recorded each year. The children included in this report were only those recruited for research studies investigating cardiovascular and neurocognitive outcomes in children with SDB, data from which has been previously published [9–15]. All children were born at term, and children with conditions such as neuromuscular diseases, craniofacial syndromes, genetic syndromes, ADHD, and Autism Spectrum Disorder, or taking medications known to affect sleep or breathing were not recruited. These included medications such as long-acting bronchodilators or other medications affecting airway patency including asthma preventer medications (e.g. fluticasone, salmeterol, budesonide, beclometasone, eformoterol, mometasone or montelukast). Children with AR were identified by a clinical diagnosis of AR recorded in their medical history. Children were otherwise healthy and not undergoing treatment with either topical nasal steroids or antibiotics on the day of the study or in the preceding 2 weeks.

Protocol

Polysomnography

All children underwent overnight attended polysomnography (PSG). Height and weight were measured and converted to a

body mass index (BMI) z-score to adjust for gender and age [16]. Electrophysiological signals were recorded using a commercially available PSG system (E-Series, Compumedics, Melbourne, Australia) using standard paediatric recording techniques [17]. Electrodes for recording left and right electrooculogram (EOG), submental electromyogram (EMG), left and right anterior tibialis muscle EMG and electrocardiogram (ECG) were attached. Thoracic and abdominal breathing movements were detected using respiratory inductance plethysmography (Pro-Tech zRIP™ Effort Sensor, Pro-Tech Services Inc., Mukilteo, WA, USA). Transcutaneous carbon dioxide ($TcCO_2$, TCM4/40, Radiometer, Denmark, Copenhagen), nasal pressure and oronasal airflow were also recorded. Oxygen saturation (SpO_2) was measured using Bitmos GmbH (Bitmos, Dusseldorf, Germany), which uses Masimo signal extraction technology for signal processing and was set to a 2-s averaging time. Paediatric sleep technologists sleep-staged and scored the PSG studies manually in 30 s epochs according to clinical practice at the time of the studies [17, 18]. A minimum of 4 h of sleep was required for children to be included in the study in order to assess SDB severity. Obstructive apnoeas were defined as a $> 90\%$ fall in airflow for $\geq 90\%$ of event duration, with continued or increased respiratory effort. Mixed apnoeas consisted of a central component followed by an obstructive component. An obstructive hypopnoea was associated with a $\geq 50\%$ fall in airflow signal for at least $\geq 90\%$ of the event, associated with an arousal, awakening or $\geq 3\%$ desaturation. Respiratory event-related arousals (RERAs) were scored where there was a discernible decrease in amplitude and flattening of the nasal pressure trace, associated with snoring, noisy breathing, elevation of the end-tidal or transcutaneous pCO_2 and/or visual evidence of increased work of breathing, leading to an arousal from sleep or $\geq 3\%$ desaturation.

The respiratory parameters from the PSG analysed for this study were the obstructive apnoea hypopnoea index (OAH) which was defined as the total number of obstructive apnoeas, mixed apnoeas, obstructive hypopnoeas and respiratory event-related arousals per hour of total sleep time (TST), average SpO_2 drop following respiratory events, SpO_2 nadir, the number of times the SpO_2 dropped by greater than 4% (ODI4), the number of times the SpO_2 dropped to below 90%, and the average $TcCO_2$.

Pollen count

Pollen counts were recorded by the Melbourne Pollen Count, School of BioSciences, University of Melbourne, using a previously published protocol [19]. In brief, a Burkard volumetric trap fitted with a 24-h sampling head (Burkard Scientific Ltd., Middlesex, UK) was used for the pollen counting. Airborne pollen was counted on a daily basis from the 1 October through to the 31 December each year. The location

of the trap, on the city campus of the University of Melbourne, conforms to the Australian Standard AS 2922–1987 for the siting of ambient air sampling units for environmental monitoring (Standards Association of Australia, Sydney, NSW). Pollen grains were trapped on a glass microscope slide coated with an adhesive (Dow Corning Sylgard 527 silicone dielectric gel) by intake of air at 10 l min^{-1} . Each day during the sampling period, the slide, attached to a rotating drum on the sampling head, was removed at around 3 pm and replaced with a fresh slide. The pollen was categorised as either ‘grass’ or ‘other pollen’. The daily concentration of pollen (in grains per m^3) was determined by staining the slide with Calberla’s stain and counting the grass and other pollen grains along a random traverse of the slide’s length and averaging these values across the entire slide.

Statistical analysis

Statistical analyses were performed using SPSS® (IBM® Statistics version 22). Data were first tested for normality and equal variance. Demographic and pollen count data were compared between children with AR and those without AR using a Student’s *t* test for parametric data and a Mann–Whitney *U* test for non-parametric data. Respiratory parameters between the groups were compared using univariate analysis of variance with asthma as a co-variate in the model. Stepwise multiple linear regressions were performed to determine whether the grass or other pollen counts, asthma, age and BMI-z-score were significant predictors of SDB severity, determined by the OAH, average SpO_2 drop, SpO_2 nadir, ODI4, the number of times the SpO_2 dropped to below 90%, and the average TcCO_2 in children with or without AR.

Results

Ninety children were included in the analysis. Demographic, respiratory and pollen count data are presented in Table 1. There were more males than females studied in both groups, which reflects the clinical population seen in the sleep centre. Of the 90 children, 14.4% (13/90) had AR only, 3.3% (3/90) had both AR and asthma and 6.7% (6/90) had asthma only. Eleven out of the 16 children with AR were on medication to treat their AR, which they stopped taking at least 2 weeks prior to the PSG, as is clinical practice in our sleep centre. Two were on a corticosteroid nasal spray only, two were on oral antihistamine only, and six were on both nasal spray and antihistamine. None of the children with asthma were on preventer medication. The inclusion of subjects with all OAH values was deliberate in order to determine whether pollen levels had an effect on SDB severity. Only including children with a high OAH would naturally prejudice the results towards high pollen counts being predictive of high SDB severity. However,

Table 1 Demographic, respiratory parameters and pollen counts for children with sleep disordered breathing, with and without allergic rhinitis

	SDB only	SDB and AR
<i>N</i> (%F)	74 (41%)	16 (1%)
Age (years)	7.1 ± 3.7	8.7 ± 2.6
BMI z-score	0.8 ± 1.2	0.5 ± 0.9
On treatment for AR	0	11
OAH (events/h TST)	1.8 (0–27.6)	2.6 (0.4–22.5)
SpO_2 nadir (%)	91 ± 5	91 ± 4
Average SpO_2 drop (%)	3.1 ± 1.3	$3.8 \pm 0.9^*$
$\text{SpO}_2 < 90\%$	0.2 ± 0.5	$0.5 \pm 0.9^*$
ODI4	1.6 ± 2.4	$4.1 \pm 6.8^{**}$
TCM (mmHg^{-1})	44.0 ± 10.8	43.3 ± 4.5
Grass (grains/ m^3) on day of PSG	8 (0–158)	12 (0–58)
Other Pollen (grains/ m^3) on day of PSG	72 (4–680)	53 (9–199)

Data presented as mean \pm std or median (min-max)

SDB sleep disordered breathing, AR allergic rhinitis, OAH obstructive apnoea hypopnoea index, SpO_2 oxygen saturation, $\text{SpO}_2 < 90\%$ the number of times oxygen saturation falls below 90% per hour of total sleep time, ODI4 the number of times oxygen saturation falls by 4% or more per hour total sleep time, TCM transcutaneous carbon dioxide

* $p < 0.05$; ** $p < 0.01$

for completeness, further analysis of the children with OSA (OAH > 1 event/h) was performed. Of the 16 subjects with AR, 12 (75%) had an OAH > 1 event/h, (33% with OAH > 1 –5, classed as mild OSA; 67% with OAH > 5 , classed as moderate/severe OSA). Of the 71 subjects without AR, 46 (65%) had an OAH > 1 event/h (50% with OAH > 1 –5; 50% with OAH > 5). OAH was higher in the children with AR, although this did not reach statistical significance. Analysis of only the children with OSA (OAH > 1) did not change the statistical results, with no significant difference ($p = 0.067$) again found between the groups. Subjects with AR had a median OAH of 4.8 (min 1.5, max 22.5); and without AR had a median OAH of 3.1 (min 1.1, max 27.6). All further analysis was conducted on the entire group of children with AR.

The average drop in oxygen desaturation following respiratory events and the number of times per hour of sleep that the oxygen saturation fell by more than 4% and to less than 90%, were significantly higher in the children with AR compared with the children without AR. Although the mean daily ‘other pollen’ count was higher when the children without AR had their PSGs, this did not reach statistical significance.

Significant determinants of sleep disordered breathing severity

In children with AR, grass pollen count was a significant determinant of OAH, SpO_2 nadir, average SpO_2 drop, $\text{SpO}_2 < 90\%$ and ODI4 (Table 2). Other pollens were significant

Table 2 Significant determinants of sleep disordered breathing severity in children with sleep disordered breathing with allergic rhinitis

	SDB and AR			
	<i>B</i>	SE	β	<i>P</i> value
OAHI	$R^2 = 0.94$			
Grass	0.20	0.05	0.51	0.003
Other pollen	0.06	0.02	0.50	0.003
SpO ₂ nadir	$R^2 = 0.59$			
Grass	−0.15	0.04	−0.78	0.001
Average SpO ₂ drop	$R^2 = 0.35$			
Grass	0.03	0.01	0.59	0.02
SpO ₂ < 90%	$R^2 = 0.83$			
Grass	0.03	0.01	0.50	0.03
Other pollen	0.01	0.003	0.47	0.02
ODI4	$R^2 = 0.91$			
Grass	0.18	0.06	0.49	0.007
Other pollen	0.06	0.02	0.47	0.009
TCM	$R^2 = 0.74$			
Other pollen	0.07	0.02	0.95	0.003

SDB sleep disordered breathing, AR allergic rhinitis, OAHI obstructive apnoea hypopnoea index, SpO₂ oxygen saturation, SpO₂ < 90% the number of times oxygen saturation falls below 90% per hour of total sleep time, ODI4 the number of times oxygen saturation falls by 4% or more per hour total sleep time, TCM transcutaneous carbon dioxide

determinants of OAHI, SpO₂ < 90%, ODI4 and TCM. For the respiratory parameters when both grass and other pollens were predictive, grass was the strongest determinant in each case. In children with AR, an increase in grass pollen of 1 grain/m³ predicted an increase in OAHI of 0.2 events/h, ODI4 of 0.18 times/h, SpO₂ < 90% of 0.03 times/h and TCM of 0.07 mmHg. Neither grass nor other pollens were significant determinants of the respiratory parameters in children without AR. A diagnosis of asthma, age and BMI z-score were not significant determinants of the respiratory parameters in children either with or without AR.

A very small increase in grass pollen of 1 grain/m³ predicted an increase in OAHI of 0.2 events/h. Over the period of this study, the local grass pollen count ranged from 0 to 234 grains/m³, and thus variations in pollen count would have a substantial impact on the OAHI. In contrast, in children who did not have AR, pollen count was not predictive of SDB severity. On days when the grass pollen count was very low (below 20 grains/m³), the average OAHI in the children with AR was correspondingly low, 1.9 events/h, which is considered clinically mild OSA. When the count was greater than 20 grains/m³, the average OAHI increased to 11.7 events/h, indicative of severe OSA. The median grass pollen count on the days when the PSG studies were conducted on the children with AR was 12 grains/m³ and ranged from 0 to 58 grains/m³, but as recorded counts can be over ten times higher than the maximum

level recorded during our study, our results may under-represent the impact of high levels of grass pollen on the day of PSG for children with AR.

Discussion

This study has identified that for children with AR, the local pollen count recorded on the day of their diagnostic PSG study significantly affected SDB severity, a finding which may inform the management of children with AR and OSA. We found that grass pollen and ‘other pollens’ were significant determinants of several aspects of SDB severity, and in each case, with the exception of expired transcutaneous CO₂, grass pollen was the strongest determinant. We also identified that for children without AR, and who are not sensitised to grass and/or other pollens, the pollen count does not influence their SDB severity on the night of their PSG.

Perennial ryegrass (*Lolium perenne*) is a valuable pasture grass planted across vast areas of southern Australia, and due to its wide distribution, ryegrass pollen is Australia’s number one outdoor allergy trigger [20]. Seasonal maximal peaks of pollen across much of southern Australia usually occur in November, although this is affected by variations in local rainfall and temperature [20]. The local regional pollen count used in this study was recorded daily from the 1 October through to the 31 December each year, which allows for variability in the peak of the pollen season across the years of data collection.

Although the average grass pollen count was 20 grains/cm³, below which the pollen count is considered very low, even levels as low as 15–20 grains/cm³ can cause symptoms in sensitive individuals. The risk for habitual snoring in children with AR may be cumulative. An immune activation in the adenoids in response to pollen, in conjunction with an imbalance of local immune cells and an abnormal inflammatory response, may lead to hypertrophy of the adenoids. Repeated stimulation of the inflammatory response causes inflammation of the nasopharynx and adjacent areas [4, 21]. Adenoid hypertrophy may not be quickly reversible, whereas nasal obstruction from mucosal oedema and secretions may be more likely to fluctuate night by night in relation to pollen load. Therefore, we suggest that the increased SDB severity associated with increased pollen counts may be related more to nasal inflammation in our cohort, rather than adenoid hypertrophy. Children with diagnosed AR are commonly receiving treatment, such as topical corticosteroid nasal sprays, antihistamines and nasal irrigation. In our study, 11 out of the 16 children with AR were being treated for their AR. As per our sleep centre’s clinical protocol, these children were required to stop taking their

medication for 2 weeks prior to their PSG. Despite this treatment, parents of the children in this cohort were still concerned enough to seek investigation for their child's snoring, and therefore, we are not able to answer the question of whether treatment for AR would have resolved the OSA.

A study of adults with AR and non-allergic rhinitis (NAR) found that AR or NAR were not risk factors for OSA severity but were associated with poor sleep efficiency and high arousal indices [22]. However, in contrast, numerous studies have reported an association between allergy and SDB in children. Ishman et al., [23] using questionnaire (OSA-18, PSQ and PDSS) data, found that children with AR, diagnosed on positive results on either a skin-prick or in vitro testing, had significantly higher scores for the likelihood of SDB than controls. Also using questionnaires to determine SDB status, Chng et al. [2] and Li et al. [24] reported that children with AR had an odds ratio for habitual snoring of 2.90 (95% CI, 2.06–4.08) and 2.9 (95% CI, 2.0–4.2), respectively, compared to children without AR. Parent-reported questionnaire-diagnosed SDB is very subjective and gives no indication of SDB severity, unlike overnight PSG, the gold standard for diagnosing SDB, which was used in our study. Using PSG, McColley et al. [3] found a significantly higher proportion of children with OSA that had a sensitivity to allergens using a multiantigen radioallergosorbent test (RAST) on serum samples. However, the RAST test used a number of unspecified food and inhalant allergens; therefore, specific sensitizations could not be determined. There have been several studies showing improvement of OSA with nasal steroids and/or montelukast [25–30]. In addition to questionnaire-reported decreased AR symptoms, Mansfield et al. [31] demonstrated that treatment of children with AR with intranasal budesonide for 6 weeks significantly reduced the mean apnoea-hypnoea index (determined by home PSG before treatment and at six weeks) from 7.6 events/h to 0.9 events/h. All of the children had a positive allergy skin prick test to a number of local environmental antigens including alfalfa, cottonwood, pigweed, and willow, amongst others, prior to the study. The presence in the region of at least some of the relevant airborne allergens for the duration of the study was determined by airborne allergen counts, which were taken on five out of every 7 days with a Rotorod sampler located at the research centre. Unlike our study, however, Mansfield et al. did not relate the level of airborne allergens on the day of the PSG to SDB severity.

Children with SDB with or without AR can also have asthma; however, asthma was not a significant determinant of SDB severity in our cohort of children.

Of the nine children with asthma who were included in this study, only three also had AR as the exclusion criteria for the research studies from which the data was obtained, precluded children with asthma who were using long-acting bronchodilators or other medications affecting airway patency including asthma preventer medications. Therefore, this result needs to be treated with caution, and further research in this area is needed with larger numbers of children with asthma and AR.

We acknowledge that our data need to be interpreted with caution given the small number of children with AR in our study. Although data were collected from 2005 until 2016, daily pollen counts were recorded only from 1 October to 31 December each year. However, these months coincide with spring and early summer, which represent the months of high pollen counts and correspondingly high AR symptomology. Further research is required to confirm our findings, as our study was cross-sectional and definitive evidence of the impact of pollens would require serial PSGs in children with AR in order to capture low and high pollen days—a study that would be logistically very difficult. Furthermore, children with AR were identified by a clinical diagnosis of AR recorded in their medical history. Although a diagnosis of allergic rhinitis due to pollen sensitivity would have been ideal, this cannot be obtained without performing skin tests or specific IgE measurements in serum. As this was a retrospective analysis, these tests were not able to be conducted and further prospective research with pollen sensitivity data is needed.

Conclusions

To our knowledge this is the first study that has identified a direct relationship between SDB severity in children with AR and the pollen count on the day of their PSG study. Grass pollen was the strongest determinant of all of the respiratory parameters that are used to determine SDB severity by physicians to inform treatment options. A child with AR who has a PSG study on a day with a low pollen count potentially may be diagnosed as having significantly less severe SDB than if that same child had their diagnostic PSG study on a day with a high pollen count. Our findings suggest that physicians need to be aware of the effect of pollen on SDB severity when considering the diagnosis and treatment of children with AR.

Acknowledgements We would like to thank Associate Professor Ed Newbigin from Melbourne University who provided the pollen count data and the parents and children who participated in this study.

Funding Funding for this project was provided by The Heart Foundation of Australia (G12M 6564), The National Health and Medical Research Council of Australia (APP1008919, APP1063500, APP491001) and the Victorian Government's Operational Infrastructure Support Program.

Compliance with ethical standards

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.

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of Monash Health and Monash University Human Research Ethics Committees and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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