Introduction

Sleep-disordered breathing (SDB) is a general term for several chronic conditions in which partial or complete cessation of breathing occurs many times throughout the night. Symptoms may include snoring, pauses in breathing and disturbed sleep. Obstructive sleep apnea syndrome (OSAS), which is by far the most common form of SDB, is characterized by episodes of complete or partial upper airway obstruction during sleep (1).

Children with OSAS are increasingly recognized as an important group of patients (2). In childhood, OSAS is most frequently due to tonsil and adenoid hypertrophy. However, obesity and anatomic alterations of the upper airways play a role (3). In childhood, the prevalence of OSAS is in the...
range of 1% to 5%, making this a relatively common disease (3,4). Screening and early treatment are recommended for children at high-risk (5,6).

The complications of OSAS are sleep fragmentation, neurocognitive, behavioural (7), cardiovascular (8) and artery hypertension (9,10). Increased levels of inflammation have been found in children with OSAS (11), linking cardiovascular pathologies with secondary oxidative stress and intermittent hypoxia (12).

Low-levels of tobacco smoke exposure have been associated with increased inflammatory biomarkers in children with asthma (13). The secondhand smoke has been associated with SDB (evidence level 3b) (14). SDB is prevalent in asthmatic children and its prevalence increased with increasing asthma severity (15). Air pollutants, such as NO₂ and particles from diesel exhausts, have adjunct effects on the pathogenesis of asthma and chronic bronchitis, which increased significantly with an increasing traffic pollution load (16). Early traffic-related air pollution exposure (particulate matter—PM₂.₅ and black carbon) was related to asthma and allergic diseases in children (17). Allergies have also been associated with airway inflammation and sleep disturbances in children (18).

Urban outdoor air pollution refers to the air pollution experienced by populations living in and around urban areas. Indoor air pollution refers to the pollutants found in indoors. The main cause of indoor air pollution is inefficient fuel combustion from rudimentary technologies. In adults, increases in SDB indices or percentage of sleep time at less than 90% O₂ saturation and decreases in sleep efficiency were all associated with increases in short-term variations in PM₁₀ from urban areas (19).

**Aims of the review**

We hypothesized that environmental air pollution can play a role in childhood SDB. The aim of this review was to find if existing researches warrant the conclusion of an association between indoor and outdoor environmental pollution (not from voluptuary habit) and SDB in children.

**Methods**

We conducted an electronic search in Medline (with PubMed interface), Scopus and the ISI Web of Science using the keywords “sleep” or “sleep apnea” or “sleep disordered breathing” and “pollution” and “children” in “Title/Abstract/Keywords”, with language restriction (non-English paper) and no date limitation to present. All the articles that responded to the search criteria were systematically reviewed by two authors (Marco Zaffanello and Laura Tenoro). Asthma and tobacco smoke’s topics were subsequently excluded because they were not pertinent to the review. The references of the selected articles were also hand-searched to identify other pertinent reports. We examined the strength of the evidence according to the Oxford Centre for Evidence-Based Medicine [2011] and the Centre for Evidence-Based Medicine [2009].

**Results**

A total of 105 published articles were identified, but 97 of these had to be excluded after an accurate reading of the title, abstract or full text (Figure 1). More specifically, studies were excluded due to: tobacco smoke (n=36), asthma...
Exposure to environmental pollutants is advocated to be a major risk factor, with increased morbidity and mortality in humans due to acute and chronic airway inflammation (28). PM$_{2.5}$, environmental pollution, in particular black carbon (a traffic-related PM$_{2.5}$ constituent), from proximity to major roadways has been associated with lower lung function in the Boston, USA, area (29). Moreover, from a study conducted at a day-care center in northeastern Seoul, Korea, indoor air pollutants resulting from nearby heavy traffic and a metro station increased the risk of allergy in children (aged 4.4±1.2 years). In addition, toluene from the indoor environment was found to be an aggravating factor. Indeed, symptoms significantly increased by 12.7% (95% CI: -0.01 to 27.1) as indoor levels of toluene increased by 1 ppb (P=0.05) (30). Moreover, long-term exposure to PM$_{10}$ and NO$_2$ has been associated with cause-specific mortality in the Dutch population (31).

Exposure to smoke impairs ciliary function in pediatric airways. Furthermore, environmental tobacco smoke exposure in children increases the incidence of upper respiratory infections, chronic sinusitis, and chronic otitis media (32). In addition, some studies found a significant association between secondhand smoke and childhood SDB (14,33,34).

Exposure to biomass smoke in rural areas may account for the higher prevalence of snoring and observed apnea by parents and grandparents of students from 20 randomly selected primary schools in urban and rural areas of Turkey. In particular, snoring and the observed apnea were more prevalent among parents and grandparents of students from rural areas [52.6% vs. 46.6%, odds ratio (OR) 1.2; P<0.001] than among those from urban areas (16.2% vs. 10.1%, OR 1.7; P<0.001) (35). Moreover, annual exposure to air pollution was associated with SDB and to a change in blood pressure among 3,762 Taiwan patients. The association between annual air pollution exposure and diastolic blood pressure accounted for high AHI (PM$_{2.5}$: OR 0.49; P=0.03) and increased BMI (PM$_{2.5}$: OR 0.52; P=0.04) (36). Unfortunately, the above research has not been conducted on a childhood population.

Exposure to indoor and outdoor pollutants may increase the incidence, severity and persistence of SDB in youth. Pathogenic mechanisms can be related to an interaction between genes and various pollutants, which leads to allergies and chronic inflammation of the upper airways (Figure 2). Although there are few studies in the topics, the results encourage further investigations. In particular, four related studies concern indoor pollution sources (21-23,25) and four studies concern outdoor pollution sources (20,24,26,27) of which one was designed for children with sickle cell anaemia (24). Two studies showed

Discussion

Exposure to environmental pollutants is advocated to be a major risk factor, with increased morbidity and mortality in humans due to acute and chronic airway inflammation (28).
Table 1 Summary of the studies regarding indoor and outdoor not-voluptuary-habit pollution and sleep disordered breathing (SDB) in children

<table>
<thead>
<tr>
<th>Reference</th>
<th>Cases</th>
<th>Nation</th>
<th>Methods of measurement</th>
<th>Evaluation of environmental pollution</th>
<th>Results</th>
<th>Design (evidence levels)</th>
</tr>
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<tbody>
<tr>
<td>(20)</td>
<td>276 children (42.9% response rate), 121 males (44%), age 9.3±2.0 years</td>
<td>Egypt</td>
<td>Sleep Disturbance Scale for Children questionnaire</td>
<td>Outdoor pollution from industrial sources; PM&lt;sub&gt;10&lt;/sub&gt; exposure in highly versus less polluted</td>
<td>✓ SDB: 9.4% (P=0.692)  ✓ Initiating and maintaining sleep: 19.9% (P=0.012)  ✓ Excessive somnolence: 24.3% (P=0.184)  ✓ Sleep hyperhidrosis: 8.3% (P=0.045)</td>
<td>Cross-sectional study (level 4)</td>
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<td>(21)</td>
<td>59 children (62.7% males; mean age 7.7±4.2 years)</td>
<td>Peru</td>
<td>Validated questionnaire</td>
<td>Indoor pollution: before and 12 months after at home installation of Inkawasi wood stove versus traditional stoves</td>
<td>✓ Snoring (52.5% vs. 18.2%, P&lt;0.0001)  ✓ Nasal congestion (33.9% vs. 1.8%, P&lt;0.0001)  ✓ Behavioural hyperactivity (28.8% vs. 3.8%, P&lt;0.002)  ✓ Night-time awakenings (42.4% vs. 1.7%, P&lt;0.0001)  ✓ Sore throat (38.3% vs. 5.5%, P&lt;0.0001)  ✓ Breathing through the mouth during the day (33.9% vs. 1.8%, P&lt;0.001)  ✓ Daytime sleepiness (21.1% vs. 1.8%, P&lt;0.003)  ✓ Falling asleep at school (14.6% vs. 0%, P&lt;0.03)</td>
<td>Prospective survey (level 3-I)</td>
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<td>(22)</td>
<td>82 children (40% boys; 8.3±3.2 years) from 56 families</td>
<td>Peru</td>
<td>Sleep-related symptom questionnaires</td>
<td>Indoor pollution: before and 2 years after at home installation of the Inkawasi stove versus traditional stoves</td>
<td>✓ Improvement in easiness to fall asleep (29.6% vs. 55.6%, P&lt;0.01)</td>
<td>Prospective survey (level 3-I)</td>
</tr>
<tr>
<td>(23)</td>
<td>77 children (11.8±1.4 years)</td>
<td>Peru (high altitude)</td>
<td>Validated questionnaire</td>
<td>Indoor pollution: particulate matter 2.5 (PM&lt;sub&gt;2.5&lt;/sub&gt;) and carbon monoxide (CO)</td>
<td>✓ Nocturnal awakenings: 48.1%  ✓ Repetitive movements and restless sleep: 46.8%  ✓ Habitual snoring: 33.8%  ✓ Positive caregiver perception of difficulty breathing during sleep (P&lt;0.0001) and presence of apneic episodes (P=0.005, respectively)</td>
<td>Cross-sectional study (level 4)</td>
</tr>
<tr>
<td>(24)</td>
<td>Sickle cell anemia (SCA) children: 95 rural, 54 urban and 19 controls</td>
<td>Kenya versus Tanzania</td>
<td>Overnight oximetry</td>
<td>Outdoor pollution: rural (Kenya) versus urban (Tanzania) areas</td>
<td>Mean: SCA Kenyan 99.0% (96.7–99.8%) vs. SCA Tanzanian 97.9% (95.4–99.3%) vs. Tanzanian controls TC 98.4% (97.5–99.1%); P=0.01  ✓ Minimum nocturnal SpO&lt;sub&gt;2&lt;/sub&gt;: 92% (86–95%) vs. 87% (78.5–91%) vs. 90 (83.5–93%), P=0.0001</td>
<td>Cohort study (level 3-II)</td>
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<td>(25)</td>
<td>A sub-group of 88996 children aged 4–6 years</td>
<td>Perth metropolitan area (Australia)</td>
<td>School-based respiratory survey (NO&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>Domestic pollutant assessments</td>
<td>Adjusted ORs of snoring by children with medium (30–60 microg/m&lt;sup&gt;3&lt;/sup&gt;) and high exposures (&gt; 60 microg/m&lt;sup&gt;3&lt;/sup&gt;) to NO&lt;sub&gt;2&lt;/sub&gt; were 2.5 (95% CI: 0.7–8.7) and 4.5 (95% CI: 1.4–14.3)</td>
<td>Cohort study (level 3-II)</td>
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<td>(26)</td>
<td>4,322 (aged 6–12 years) children attending public schools</td>
<td>Tehran, Iran</td>
<td>Questionnaires</td>
<td>Officially published air quality measures by the governmental Air Pollution Control Company</td>
<td>Higher habitual sno-ring frequencies among children residing in neighbourhoods with greatest pollution (24.5% and 12.1% (level 3-I) in South and Central neighbourhoods versus 7.0% and 7.7% in North and East neighbourhoods, respectively)</td>
<td>Cohort study (level 3-II)</td>
</tr>
<tr>
<td>(27)</td>
<td>754 children</td>
<td>Varese province, Italy</td>
<td>Embla’s Embletta National officially published air Gold sleep system quality measures (PM&lt;sub&gt;10&lt;/sub&gt; and NO&lt;sub&gt;2&lt;/sub&gt;)</td>
<td>SDB was more severe in the South Varese province, close to the airport</td>
<td></td>
<td>Cohort study (level 3-II)</td>
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</table>
reductions in SDB following successful air-quality home-based interventions (21,22). Three studies come from the same research team (21-23); but the places of the studies were not the same, so they evaluated different cohorts. However, one communication reported higher severity of SDB in children living close to the airport (27) and two studies showed higher habitual snoring among children living in place with greater environmental pollution (25,26).

A possible limitation comes from one study: sickle cell anemia children are non-healthy and hypoxemic by definition (24). Moreover, other possible limitation of these studies is that they mainly used questionnaires to screen for SDB in children exposed to environmental pollution, this is less reliable as a real measurement of SDB level (37). Therefore, some research has supported the validity of questionnaires and the convergence of polysomnography and questionnaires for assessing SDB (38,39). It is not easy to conduct studies on air pollution and its impact on health in general and especially, on a complicated, multifactorial disease like SDB.

There are a few medical studies on children living in the most industrialized countries, although the global impact of city traffic and industries on the health of the human population is often an issue. Moreover, exposures assessed among the studies are very heterogeneous, making a systematic review more challenging. That heterogeneity of exposure measurements should be acknowledged.

Conclusions

There is currently some interesting information in the literature concerning SDB in children exposed to indoor/outdoor pollution. In particular, some studies reported significant differences between areas with higher and lower pollutants and the interventions on indoor pollution reduced sleep-disordered breathing in children. Therefore, although the relevance of the argument is high, the number of studies and the interest in the subject seems at this time quite limited.

Acknowledgements

None.

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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31. Liu WT, Lee KY, Lee HC, et al. The association of annual air pollution exposure with blood pressure among patients...