



CLINICAL REVIEW

Influence of asthma on sleep disordered breathing in children: A systematic review



Pablo E. Brockmann*, Pablo Bertrand, Jose A. Castro-Rodriguez

Department of Pediatrics, School of Medicine, Pontificia Universidad Catolica de Chile, Chile

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SUMMARY

The objective of this study was to perform a systematic review for the association between asthma and sleep disordered breathing (SDB) in children. We performed an electronic search in Medline, Embase, CINAHL, LILACS and Cochrane databases. Study selection criteria: children <18 y of age with diagnosis of asthma and SDB. Primary outcomes: odds ratios (OR) and 95% confidence intervals [95%CI] of asthma for SDB were calculated. There were $n = 968$ citations identified, of them $n = 17$ studies were selected, which included $n = 45\,155$ (53% males) children. All included studies defined asthma and SDB based on questionnaires, and only two performed a sleep study for diagnosing obstructive sleep apnea. Mean age was 8.6 ± 2.5 y. SDB was significantly more frequent in children with asthma compared with non-asthmatics: 23.9% vs 16.7% respectively, $p < 0.0001$. Children with asthma had a significantly higher risk for SDB: OR 1.9 [1.7; 2.2]. This systematic review showed evidence of a significant association between asthma and SDB in children. Asthma seems to be a significant risk factor for developing SDB. However, the minority of the studies based the diagnosis of SDB on polysomnography, considered the current gold standard for SDB. The physiological and temporal relationships between both conditions should be addressed in future cohort studies.

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Introduction

Asthma is among the most prevalent chronic diseases in children [1]. The prevalence of asthma has rapidly increased worldwide over the last decades [2]. Similarly to the increase of the prevalence of asthma, snoring and sleep disordered breathing (SDB) have also increased reaching similar prevalence than asthma [3].

On the other hand, upper and lower airway inflammation is related to allergic diseases like rhinitis and asthma, and the release of inflammatory molecules [4]. Among these inflammatory mediators, cystenil leukotrienes have been identified in asthma [5] and also SDB [6]. Furthermore, the presence of cystenil leukotrienes seems to play an important role in the development of adenotonsillar hyperplasia that is one of the leading factors for developing SDB [7].

Abbreviations: OR, odd's ratio; SDB, sleep disordered breathing; SD, standard deviation; ISAAC, international study on asthma and allergies in childhood; PEF, peak expiratory flow; PSQ, pediatric sleep questionnaire; RSV, respiratory syncytial virus.

* Corresponding author. Lira 85, 5to Piso, 8330074 Santiago, Chile.

E-mail address: pbrockmann@med.puc.cl (P.E. Brockmann).

This similar increase in prevalence and the fact that both are diseases that are associated with a common inflammation of the airway [8], have led to the search of an association between asthma and SDB [9]. Although there have been attempts to demonstrate an association between asthma and SDB in children, there has been no state of the art systematic review to support this potential association. Therefore, we performed the present systematic review in order to analyze all available evidence for an association between asthma and SDB in children.

Methods

Search and selection criteria

We developed individual search strategies for each of the following bibliographic databases: Medline (1950–present), Embase (1988–present), CINAHL (1982–present), and LILACS (1986–present). The strategy used several combinations of searches concerning following keywords: asthma OR wheezing AND sleep apnea OR snoring OR sleep disordered breathing. We applied also individual limits for detecting only studies on subjects

younger than 18 y, without language restriction. All references were managed by reference manager software (Review Manager 5.1.2, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). All database searches were started in January 2012, with an update in September 2013. Reference lists from eligible studies and review articles were crosschecked to identify additional studies. The detailed search strategy is available from the authors.

Study selection

Types of studies

All types of studies that aimed to establish an association between asthma and SDB in children were considered.

Participants

Studies including children <18 y of age were eligible for inclusion. Studies that included more than 20% of subjects with any other chronic underlying diseases (i.e., genetic/metabolic disorders, craniofacial malformations, or neurological/neuromuscular disorders) were excluded.

Target conditions

We accepted studies that clinically defined asthma as a recurrent, chronic condition, characterized by intermittent or persistent wheezing. Questionnaire based (e.g., International Study on Asthma and Allergies in Childhood (ISAAC) questionnaire [1,10]) diagnosis of asthma was also accepted. SDB was defined according to the International Classification of Sleep Disorders 2nd edition [11], and accepted all forms of SDB (i.e., habitual snoring, upper airway resistance syndrome, and obstructive sleep apnea) as target diagnoses. The diagnosis of SDB was accepted when based on questionnaire, clinical examination, or polysomnography.

The primary outcome of the present study was the frequency of asthmatic subjects with SDB. Secondary measures were the odd's ratios (OR) and their 95% confidence intervals [95%CI] for SDB based on the diagnosis of asthma. A differentiated evaluation of those studies that objectively assessed asthma and SDB diagnosis on spirometry and polysomnography, respectively, was planned.

Data extraction

This systematic review was performed according to criteria established by the preferred reporting items for systematic reviews and meta-analyses (PRISMA) [12] and the meta-analysis of observational studies in epidemiology (MOOSE) guidelines [13]. Titles and abstracts of records retrieved by the electronic searches were independently screened by three reviewers with experience in pediatric sleep medicine and asthma (PEB, PB, JAC). After obtaining the full text of potentially relevant articles eligibility was discussed. Disagreement between reviewers was resolved by group discussion.

Heterogeneity of the studies was assessed by the I^2 test (<40% was accepted as not relevant). Risk of bias was also investigated by the observation of Funnel plots. Quality of the included studies was assessed with the Newcastle–Ottawa scale (NOS) for assessing the quality of nonrandomised studies (http://www.ohri.ca/programs/clinical_epidemiology/oxford.htm).

Extracted data were managed with appropriate software (Review Manager 5.1.2, The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark) and frequencies, ORs of SDB were calculated. Forest plots were constructed for the association between asthma and SDB. Descriptive statistics (mean, standard deviation [SD], median, minimum, maximum) were used to summarize studies' characteristics, and results. Comparisons of

frequencies and ORs of SDB in children with asthma compared with controls were conducted with the non-parametric Mann–Whitney–*U* test.

Results

From $n = 968$ citations identified, $n = 17$ studies [8,14–29] fulfilled the inclusion criteria and were selected after discussion (Fig. 1). Selected studies included $n = 45\,155$ (53% males) children, the mean (SD) age was 8.6 (2.5). Six studies were conducted in Asia [15,18,19,29–31], five in Europe [8,16,17,23,27], four in the US [20,22,25,26], and two in Australia [24,28]. Almost all studies assessed asthma and SDB based on questionnaires or clinical history, there was only one study that performed polysomnography [25] and one a home cardiorespiratory polygraphy [26]. The ISAAC questionnaire was specifically used in five studies [17,22,28–30], the remaining used similar items or unstructured questionnaires for assessing asthma. Spirometry was performed only in four studies [17,20,22,26]. Details on the description of the included studies are given in Table 1. Sensitivity analysis between age groups (like pre-schoolers, school aged children or adolescents) or gender was not possible, as no study provided differentiated results analysis concerning the association between asthma and SDB.

Eight of the included studies [14,16,18,19,21,24,25,32] intended to investigate the prevalence of SDB, and asthma was assessed among other studied risk factors. In contrast, there were $n = 8$ studies [8,15,17,22,23,26,28,29] that investigated risk factors for asthma. One study analyzed nocturnal symptoms of asthma [20], among which data on snoring were extractable.

Median (minimum–maximum) SDB prevalence was 23.9% (7.1%–77.3%) in children with asthma compared to 16.7 (5.1–69.5)% in those without (p -value <0.0001). Details on the frequencies are given in Table 1.

Quality assessment

Quality assessment is shown in Fig. 2. Median obtained NOS score was 5/10. Lowest scores were obtained in the question concerning the ascertainment of exposure (see Fig. 2), only one study obtained data based on secure records or structured interviews. All other studies obtained data based on parental questionnaires or

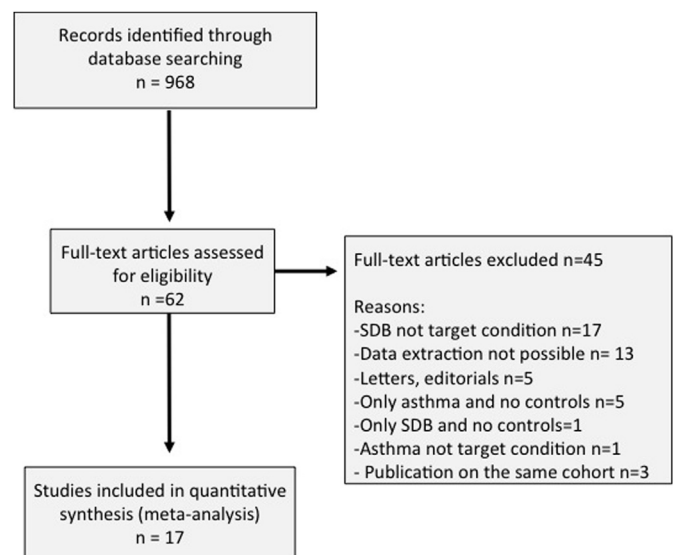


Fig. 1. Study selection process.

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