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Risk of invasive pneumococcal disease in children and adults with asthma: A systematic review

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ABSTRACT

Background: The Advisory Committee on Immunization Practices (ACIP) recommended the inclusion of asthma as a high-risk condition that should warrant pneumococcal vaccination, but the National Advisory Committee on Immunization (NACI) in Canada has not yet done so. We aimed to determine the risk of invasive pneumococcal disease (IPD) in patients with asthma.
Methods: We searched Ovid Medline, EMBASE, Classic EMBASE, PubMEd and Cochrane for articles published between January 1990 and February 2013, using the MeSH terms pneumococcal infections/or invasive pneumococcal disease and asthma. Google Scholar was used to retrieve articles citing the seminal article by Talbot et al. Articles were included if they were population-based studies that evaluated the relationship between IPD and asthma. Two authors independently assessed all titles and abstracts. All potentially relevant articles were retrieved as full text and assessed for inclusion.
Results: The combined searches yielded 376 articles, which were reviewed by title and abstract. At this stage, 330 articles were excluded; 40 articles were excluded at the full article review stage – leaving 6 articles. Two additional articles were found through Google Scholar. The evidence reviewed consistently showed a positive association between asthma and risk of IPD. However, the magnitude of this effect was heterogeneous with adjusted odds ratios ranging from 6.7 (95% CI 1.6–27.3) in adults >18 years to 1.7 (95% CI 0.99–3.0) in individuals aged 2–49 with low-risk asthma.
Conclusion: The positive association between asthma and risk of IPD supports the addition of asthma as a high-risk condition warranting pneumococcal vaccination. Data on vaccine effectiveness in this population is needed.

1. Introduction

Streptococcus pneumoniae (pneumococcus) is the causative agent of invasive pneumococcal disease (IPD), which includes bacteremia, meningitis, and/or pneumonia with bacteremia. Fifteen of the ninety-two pneumococcus serotypes account for a major cause of IPD-related morbidity and mortality worldwide [1]. It is known that young children, the elderly and those with certain underlying medical conditions, like severe asthma, are at increased risk of IPD [2]. As such, the Canadian National Advisory Committee on Immunizations (NACI) has recommended that adults with asthma associated with chronic obstructive pulmonary disease (COPD), emphysema, or those who need prolonged systemic corticosteroid receive one dose of the 23-valent pneumococcal polysaccharide vaccine (PPV23). Children aged 2 years and over with asthma requiring prolonged systemic corticosteroid should receive one dose of pneumococcal conjugate vaccine (13-valent) if not previously vaccinated, followed by PPV23 [3].

Recent studies reported a positive association between asthma (regardless of severity) and IPD [4–9]. Currently in Canada, there is no recommendation to vaccinate asthmatics in general. A risk-based approach to pneumococcal vaccination using PPV23 could prevent substantial morbidity in the entire asthmatic population. Recent statistics show that as of 2011, there were 1,785,173 asthmatics in Canada between the ages of 20 and 64, representing close to 10% of the Canadian population in this age group [10]. Given the recent data and the prevalence of asthma in Canada, we aimed to conduct a systematic review of the literature to determine if asthma significantly increases risk of IPD, providing support for a vaccination policy to prevent IPD for asthmatics in Canada.

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2. Methods

2.1. Search strategy

In collaboration with a research librarian, we searched the following four electronic databases: Ovid Medline, EMBASE (1966–2013 Week 7), Classic EMBASE (1947–2013 February), PubMEd and Cochrane for articles published between January 1990 and February 2013. For Medline searches, we used the MeSH Headings: pneumococcal infections/OR invasive pneumococcal disease AND asthma OR asthma/. Analogous terms were used to conduct the EMBASE, PubMed and Cochrane searches. Appendix A details the full search strategy. We also hand-searched Google Scholar for articles citing the Talbot et al. study [4], as this is the seminal study where asthma was described as a risk factor for IPD.

2.2. Inclusion and exclusion criteria

Articles were included if they were population-based studies that evaluated the relationship between asthma and IPD and, either exclusively (i.e. studies that evaluated only asthma as a risk factor for IPD) or inclusively (i.e. studies that evaluated the relationship between asthma, among other factors, and IPD). Only studies published between January 1990 and February 2013 in either French or English were included. Articles were excluded if they presented secondary data, were policy recommendations, or did not evaluate asthma as a risk factor for IPD; however, references from these articles were perused.

2.3. Assessment of studies

Two authors (CB and CQ) independently assessed all titles and abstracts identified by the search strategy described above. All potentially relevant articles, chosen by consensus between the two authors, were retrieved as full text and assessed by CB and CQ for inclusion. All included studies were given a quality ranking by CB based on the ranking devised by Harris et al. [11] and adapted by NACI. This quality schedule scores across three dimensions labeled as "good", "fair", and "poor" based on the number of flaws present in study design methodology. It was concluded that a meta-analysis of the selected studies was not justifiable as included studies differed greatly in their definition of IPD, asthma, and outcome measures.

3. Results

3.1. Search results

The combined searches yielded 376 articles, which were reviewed by title and abstract. During this process, 330 articles were excluded either because they were not published between 1990 and 2013 or did not explicitly discuss the relationship between asthma and IPD. As such, 46 articles remained for full-text review. We excluded 40 articles that did not fulfill inclusion criteria (Fig. 1). Eight articles were kept after full-text review; six articles [4–9] from the database search and two articles [12,13] that were missed by our database search but identified from Google Scholar (Table 1). Of the included studies there were: six case–control studies [4,5,7,8,12,13], a retrospective population-based surveillance study [9] and a prospective population-based surveillance study [6]. Three of the six studies evaluated risk of IPD in asthmatic children (<18 years old [9], <17 years old [13], 3–59 months old [8]); three studies only included adult participants (>18 years old) [7,12,6], and two studies included both adults and children [4,5]. It should be noted here that the study by Juhn et al. [5] was included because it met inclusion criteria (it was published in 2008); however, this study uses data from before the inclusion period outlined in our protocol. It was included in our analysis regardless of the potential differences in asthma treatment because the data in this article is relevant to our study question and the study methodology is valid.

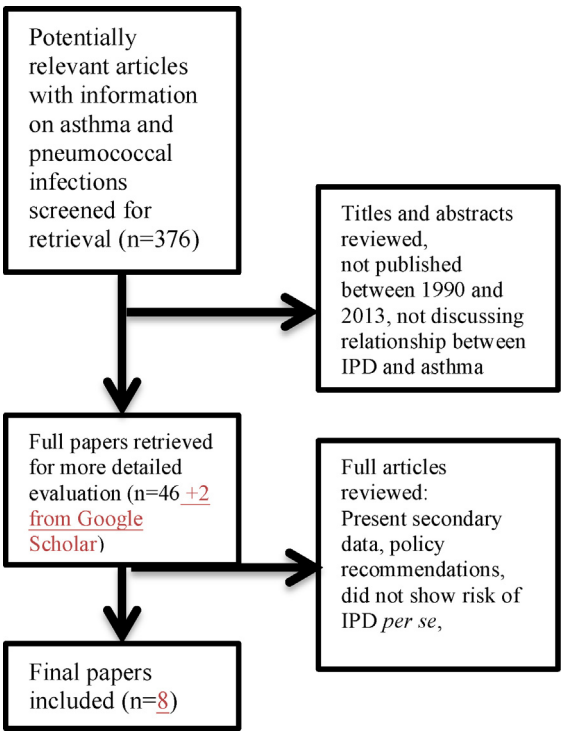

Fig. 1. Description of search and inclusion/exclusion process.

3.2. Quality assessment

Case–control studies and surveillance studies were evaluated based on the ascertainment and selection of cases and controls, the unbiased treatment of cases and controls with respect to inclusion/exclusion criteria and diagnostic testing procedures, and on the attention to potential confounding variables [11]. No included studies received a quality assessment score of "poor". Six studies [4,7–9,6] received a grade of "good". Two studies [5,12] received a grade of "fair".

4. Retrieved studies

4.1. Pediatric studies

Pilishvili et al. [8] conducted a population- and lab-based case–control study with a population of 3924 U.S. children aged 3–59 months. Cases were identified through routine Active Bacterial Core (ABC) surveillance of IPD in California, Colorado, Georgia, Minnesota, New York, Oregon, Tennessee and Connecticut. Three controls were matched to each case on the basis of age and mother's residence zip code at time of birth. Health care providers, "from whom children reportedly received routine medical care and immunizations" [8], ascertained information on underlying illnesses, including asthma status, for all study participants. This study found that IPD case patients with non-PCV7 type IPDs were more likely than controls to have asthma (OR 1.5; 95% CI 1.1–2.1).

Hsu et al. [9] conducted a retrospective population-based study to determine the underlying conditions predisposing Massachusetts' children aged <18 years old to IPD in the "PCV-7 vaccine era" between October 1, 2001 and September 30, 2007. Cases were ascertained using microbiology laboratory reports. Cases classified