Vaccine xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Vaccine

journal homepage: www.elsevier.com/locate/vaccine

Review

The impact of 10-valent and 13-valent pneumococcal conjugate vaccines on hospitalization for pneumonia in children: A systematic review and meta-analysis

Cristiano Alicino, Chiara Paganino *, Andrea Orsi, Matteo Astengo, Cecilia Trucchi, Giancarlo Icardi, Filippo Ansaldi

Department of Health Sciences, University of Genoa, Italy

ARTICLE INFO

Article history:
Received 31 January 2017
Received in revised form 28 August 2017
Accepted 1 September 2017
Available online xxxx

Keywords:
Pneumonia
CAP
Streptococcus pneumoniae
Hospitalization
Prevention
Vaccines
PCV10
PCV13
Meta-analysis

ABSTRACT

Background: This systematic review and meta-analysis aimed at summarizing available data on the impact of PCV10 and PCV13 in reducing the incidence of CAP hospitalizations in children aged <5 years.
Methods: A systematic search of the literature was conducted. We included time-series analyses and before-after studies, reporting the incidence of hospitalization for pneumonia in the periods before and after the introduction of PCV10 or PCV13 into the immunization program. Pooled estimates of Incidence Rate Ratio (IRR) were calculated by using a random-effects meta-analytic model. Results were stratified according to age-groups (<24 months and 24–59 months) and case definitions of pneumonia (clinically and radiologically confirmed pneumonia).
Results: A total of 1533 potentially relevant articles were identified. Of these, 12 articles were included in the analysis. In children aged <24 months, the meta-analysis showed a reduction of 17% (95%CI: 11–22%, p-value < 0.001) an of 31% (95%CI: 26–35%, p-value < 0.001) in the hospitalization rates respectively for clinically and radiologically confirmed pneumonia, respectively, after the introduction of the novel PCVs.
Results: In children aged 24–59 months, the meta-analysis showed a reduction of 9% (95%CI: 5–14%, p-value < 0.001) and of 24% (95%CI: 12–33%, p-value < 0.001) in the hospitalization rates for clinically and radiologically confirmed pneumonia, respectively, after the introduction of the novel PCVs.
Results: High heterogeneity was detected among studies evaluating the hospitalization rate for clinically and radiologically confirmed pneumonia.
Conclusions: The results of this study revealed a significant impact of PCV10 and PCV13 in reducing the hospitalizations for pneumonia, particularly in children aged <24 months and for radiologically confirmed disease. Further appropriately designed studies, comparing the impact of PCV10 and PCV13, are needed in order to obtain solid data on which to establish future immunization strategies.

Contents

Abbreviations: CAP, community-acquired pneumonia; IPD, invasive pneumococcal disease; IRR, incidence rate ratio; PCV, pneumococcal conjugate vaccine; PCV7, 7-valent pneumococcal conjugate vaccine; PCV10, 10-valent pneumococcal conjugate vaccine; PCV13, 13-valent pneumococcal conjugate vaccine; Sp, *Streptococcus pneumoniae*; VE, vaccine effectiveness; WHO, World Health Organization; 95%CI, 95% confidence interval.

* Corresponding author at: Department of Health Sciences, University of Genoa, Via Pastore 1, 16132 Genoa, Italy.
E-mail address: chiara.paganino@edu.unige.it (C. Paganino).

http://dx.doi.org/10.1016/j.vaccine.2017.09.005
0264-410X/

1. Introduction

Community-acquired pneumonia (CAP) represents a significant public health problem worldwide and a leading cause of death, especially in children. In 2010, 120 million episodes of pneumonia were globally estimated in children aged <5 years; the incidence in this age group is calculated in 0.29 episodes per child-year in developing and 0.05 episodes per child-year in developed countries [1–3]. Moreover, nearly 14 million of pneumonia cases progressed to severe episodes, and 1.3 million led to death [2,3]. The highest proportion of deaths (81%) was recorded mainly in children under 2 years of age living in low and middle-income countries [3].

Streptococcus pneumoniae (Sp) is the most frequent etiologic agent of bacterial CAP cases (2.2–50.9%) among children aged under five years and can cause serious complications requiring recourse to appropriate medical care and hospitalization [4].

Childhood vaccination against Sp was first recommended by the World Health Organization (WHO) in 2007 and is now the main means of preventing pneumococcal disease, together with other pneumonia control measures, such as appropriate case management, promotion of exclusive breastfeeding for the first 6 months of life and the reduction of known risk factors [5].

By the end of 2015, pneumococcal vaccines had been introduced into the standard infant immunization schedule in 129 countries, and the global coverage was estimated at 37% [6]. Pneumococcal conjugate vaccines (PCVs) have been proved to be a highly efficacious means of protecting children younger than 2 years of age against severe forms of pneumococcal disease, such as pneumonia, meningitis and bacteremia [7]. The first pneumococcal conjugate vaccine was a 7-valent pneumococcal polysaccharide-protein conjugate vaccine (PCV7), licensed by the Food and Drug Administration for use in children in 2000 [8].

Since 2010, two novel PCV formulations protecting against 10 (PCV10) and 13 (PCV13) Sp serotypes have become available for use in children, offering better coverage for Sp serotypes that commonly cause disease in low- and middle-income countries [9,10]. Several studies have demonstrated the efficacy of PCV7 in reducing CAP hospitalizations in children, mostly in developed countries [11–16]. Since the introduction of PCV10 and PCV13 into national immunization programs, a number of studies have evaluated the impact of these formulations in terms of reduction of the burden of CAP.

This systematic review and meta-analysis aimed primarily at summarizing available data on the impact of PCV10 and PCV13 in reducing the incidence of CAP hospitalizations in children aged <5 years. The secondary objective was to study whether PCV10 and PCV13 displayed a different impact on CAP hospitalizations in the same age group.

2. Methods

We conducted a systematic review of the literature and meta-analysis based on data from impact studies that evaluated, in terms of rate ratio, the incidence reduction of hospitalization for clinical CAP and for radiologically confirmed pneumonia in children younger than 5 years of age in the period before and after the introduction of PCV10 or PCV13.

2.1. Data sources and searches

A literature search using the three different online medical databases (PubMed, SciELO and Lilacs) was conducted in order to identify relevant articles published up to December 15th 2016.

The syntax and keyword combinations used to develop the search string are presented in Table S1.

References from the selected studies were manually examined to identify any other potentially suitable publications.

2.2. Inclusion and exclusion criteria

We included all studies published after the year 2000, when the first conjugate pneumococcal vaccine was licensed. The reports were in English, Spanish and Portuguese, but no restrictions were placed on language.

Care was taken to ensure that the studies selected did not result in duplication of data. In the case of multiple reporting of the same data, we planned to group the results and reported them as extracted from a single study. Review articles, posters, oral presentations at conferences, abstracts and editorials were excluded.

In the systematic review and in the meta-analysis, we included quasi-experimental studies, namely time-series, interrupted time-series and before-after studies in which the incidence of hospitalization for pneumonia was calculated and the periods before and after the introduction of PCV10 or PCV13 into the immunization program were compared, regardless of the length of the periods of observation before and after the introduction of the novel PCVs. We included both studies conducted in settings in which the introduction of PCV10 or PCV13 was not preceded by the use of PCV7 and studies carried out in settings in which PCV7 was introduced into the immunization program and then replaced by PCV10 or PCV13.

Please cite this article in press as: Alicino C et al. The impact of 10-valent and 13-valent pneumococcal conjugate vaccines on hospitalization for pneumonia in children: A systematic review and meta-analysis. Vaccine (2017), http://dx.doi.org/10.1016/j.vaccine.2017.09.005