



A nationwide study on the impact of pneumococcal conjugate vaccination on antibiotic use and ventilation tube insertion in Denmark 2000–2014



Michael Frantz Howitz^{a,*}, Zitta Barrella Harboe^{b,c}, Helene Ingels^d, Palle Valentiner-Branth^e, Kåre Mølbak^e, Bjarki Ditlev Djurhuus^{f,g}

^a Department of ENT Head & Neck Surgery, Nordsjællands Hospital, Dyrehavevej 29, 4000 Hillerød, Denmark

^b Department of Microbiology and Infection Control, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark

^c Department of Infectious Diseases, Rigshospitalet, Blegdamsvej 9, 2100 Copenhagen Ø, Denmark

^d Department of Pediatrics, Næstved Hospital, Ringstedgade 61, 4700 Næstved, Denmark

^e Department of Infectious Disease Epidemiology, Statens Serum Institut, Artillerivej 5, 2300 Copenhagen S, Denmark

^f Epidemiology, Biostatistics and Biodemography, University of Southern Denmark, J.B. Winslows Vej 9 B, 5000 Odense C, Denmark

^g Department of ENT Head & Neck Surgery, Zealand University Hospital, Lykkebækvej 1, 4600 Køge, Denmark

ARTICLE INFO

Article history:

Received 9 October 2016

Received in revised form 31 August 2017

Accepted 1 September 2017

Available online 18 September 2017

Keywords:

PCV7

PCV13

VTI

Ventilation tube insertion

Antibiotic

Upper respiratory diseases

ABSTRACT

Introduction of Pneumococcal Conjugated Vaccines (PCV) in national immunization programs have been successful in reducing the number of invasive and lower respiratory pneumococcal infections. The impact of the vaccines on upper respiratory infections caused by pneumococci is less clear although these account for most pneumococcal infections. In this study, we used likely proxies for respiratory infections in children, such as antibiotic use and ventilation tube insertions (VTI), to estimate the impact of the vaccine on a national level. The study was designed as a population-based retrospective observational study, comparing trends in the incidence rate of antibiotic prescriptions and VTIs in the period 2000–2014, where PCV7 was introduced in 2007 and PCV13 in 2010.

The introduction of PCV7 and PCV13 correlated with changes in the incidence rate from an almost steady increase in prescription of antibiotics in the pre-PCV period to a decreasing incidence for all children age 0–15 years. The 2.4 DDD per person year in 2014 was at almost the same level of antibiotic use as in 2000 at 2.3 DDD per person year. Similar patterns were observed in the mostly vaccinated age groups below 5 years of age. For VTI we observed a decreasing incidence rate in the years following introduction of PCV13 ending with a slightly higher incidence at 35 per 1000 person years in 2014 compared to 31 in year 2000.

We conclude that the steady increase in antibiotic use and VTI in the pre-PCV period have been partially reversed to near year 2000 levels after the introduction of PCV. This indicates that implementation of pneumococcal vaccines in the Childhood Vaccination Programme has likely reduced the incidence of upper respiratory diseases due to pneumococci in Denmark.

© 2017 Elsevier Ltd. All rights reserved.

Abbreviations: AOM, acute otitis media; ATC, anatomical therapeutic chemical classification system; CI, confidence interval; DDD, defined daily dose; DNHR, Danish national health register; IPD, invasive pneumococcal disease; NCSF, NOMESCO classification of surgical procedures; OME, otitis media with effusion; PCV, pneumococcal conjugate vaccines; rAOM, recurrent acute otitis media; SKS, sygehusvæsnets klassifikations system; VTI, ventilation tube insertion; WHO, world health organization.

* Corresponding author.

E-mail address: mfhowitz@gmail.com (M.F. Howitz).

1. Introduction

Since the introduction of pneumococcal conjugate vaccines (PCV) in infant immunization programs, many countries have seen a decline in invasive pneumococcal disease (IPD; sepsis and meningitis) [1]. In Denmark, the 7-valent PCV was introduced in October 2007 and replaced by the 13-valent PCV during 2010 [2,3]. After the introduction of PCV13 the incidence of IPD in the total population decreased by 21% and by 71% among children <2 years [4]. However, respiratory tract infections, i.e. acute otitis media

(AOM), pneumonia, and sinusitis are by far the most common conditions caused by *S. pneumoniae*. In a recent Canadian study, it was estimated that only 2% of the total cost related to pneumococcal disease was attributable to invasive disease, while 98% of the costs came from treatment of noninvasive infections; among which AOM and ventilation tube insertions (VTI) represented 84% [5].

A Cochrane review on randomized controlled trials on the effect of PCV7 on AOM found a modest beneficial vaccine effect restricted to healthy children with a low risk of AOM [6]. In an ecological study, Groth et al. found no decrease in the incidence rate of VTI in children <2 years of age in the Central Denmark Region after the introduction of PCV7 [7]. The objective of the present study was to estimate the impact of the introduction of PCV7 and PCV13 on the use of antibiotics as a proxy for respiratory infections and VTI as a proxy for recurrent AOM (rAOM).

2. Material and methods

2.1. Study design

The study was designed as a population-based retrospective observational study, with trends in the incidence rate of VTIs and antibiotic prescriptions for the period 2000–2014 as main outcome measures.

2.2. Study population

The study population comprised all children aged 0–15 years in Denmark from 2000 to 2014. During the period the study population varied between 1.04 and 1.08 million [8]. The national coverage of PCV for three doses followed an increasing trend from 69% in 2007, 87% in 2008 and was 90% in 2014 on a par with the coverage of the DTaP-IPV/Hib/DTaP-IPV/HibHbv vaccination that is administered concomitantly. Previously, the coverage of PCV was 1–2% points lower [9].

2.3. Material

We obtained data from the three national registers described below. The Danish health care system is tax-based providing universal coverage and equal access for all residents [10]. Data between registries were combined using the unique personal identification number assigned to all Danes.

2.4. The Danish National Prescription Registry

The Danish National Prescription Registry (DNPR) contains individual-level data on all prescription drugs sold in Danish community pharmacies since 1994. Registration is reimbursement-driven as well as required by law. The register is thus considered to be of high quality and unique in an international perspective [11]. Aggregated data from DNPR on different ATC drug groups since 1999 is available online, e.g. as defined daily doses (DDD). Data on systemic antibiotics (ATC code J01) in this study were downloaded from the website [12]. Nearly all antibiotics prescribed in the study period were referable to specific persons, and this proportion increased from 95% to 97% between 1999 and 2013. The remaining 3–5% are antibiotics given in hospitals, which is not referable to a specific person in this registry, and antibiotics prescribed for physicians to have in their clinic or doctors bag. In Denmark the two antibiotic mainly prescribed to children and adults are penicillin and amoxicillin [13].

2.5. The Danish national health service register

The Danish National Health Service Register (NHSR) contains data from the primary health care, including private ear-, nose- and throat clinics, since 1990. Everyone residing in Denmark is covered by the Health Insurance Service and data are generated through the practicing medical specialists' invoices to the regional health administration [14]. The quality of the NHSR is considered to be good [15]. We obtained data on VTI's (reimbursement codes 3009, 3109, 6432 and 6433 according to the Danish Classification of Surgical Procedures and Therapies).

2.6. The Danish National Patient Register

The Danish National Patient Register (NPR) was established in 1977 and registration of all admissions to public hospitals has since been mandatory. Since 1995 out-patient visits have also been registered. An upcoming of a private healthcare sector in Denmark from around year 2000 necessitated registration from private hospitals too, which in full became compulsory in 2003. For the applied period, registration of surgical procedures was performed using the "Classification of Surgical Procedures and Therapies" from the Nordic Medico-Statistical Committee and data on VTI were drawn using the surgical code KDCA20 [16,17]. The NPR is considered to be the finest of its kind internationally and for codes concerning otosurgery the positive predictive value has been estimated to 98% [16,18].

2.7. Data analyses

In the estimation of incidence rates, annual mean populations were applied. Incidence rate ratios were examined with Poisson regression models by inserting linear splines at relevant calendar years. Data on the background population was drawn from Statistics Denmark's homepage with aggregated data stratified by calendar year, age in one-year-groups and sex [10].

In the presented incidence rates in 0–15-year-olds, direct age standardization using WHO's population estimation for 2000–2025 was applied [19] to correct for any temporal changes in the age distribution in the population. Direct age standardization was applied to make comparison of incidence rates with future studies possible.

Stata version 14 (StataCorp, College Station, TX) was used for the statistical analysis. The study was approved by the Danish Data Protection Agency (J.no 2015-41-3711). No other approvals were needed for this registry based study.

3. Results

3.1. Antibiotics

From 2000 to 2014 a total of 41,466,000 defined daily doses (DDD) antibiotics were purchased to 0–15-year-olds in Denmark.

Throughout the pre-PCV period (2000–2007), a gradual increase in the use of antibiotics was observed (Fig. 1). In 0–15-year-olds the age adjusted annual incidence rate increased from 2.3 DDD per person year in 2000 to 2.9 per person year in 2007. In 0–15-year-olds the Poisson regression analysis estimated an annual increase of 2.6% (95% CI 2.6–2.6%) in the period (Table 1). Similar annual increases were estimated among one-year age-groups among preschool children (Table 1).

The introduction of PCV7 in October 2007 was followed by a temporal decrease in the use of antibiotics (Fig. 1). In 2009 among 0–15-year-olds the age adjusted annual incidence rate decreased to 2.5 DDD per person year. The Poisson regression analysis esti-

Download English Version:

<https://daneshyari.com/en/article/5536860>

Download Persian Version:

<https://daneshyari.com/article/5536860>

[Daneshyari.com](https://daneshyari.com)