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Pertussis vaccination in infancy lowers the incidence of pertussis disease and the rate of hospitalisation after one and two doses: Analyses of 10 years of pertussis surveillance

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ABSTRACT

Objectives: Shortly after pertussis vaccination was reintroduced in Sweden in 1996, an intensified pertussis disease surveillance programme was set up. In this study, we report on in-depth analyses of age–dose–number-specific incidences and the rate of pertussis hospitalisation for children with no, 1 or 2 doses of an acellular pertussis vaccine before pertussis disease. Vaccine coverage, the timeliness of childhood vaccination and the effect of later than scheduled pertussis vaccination(s) are also examined.
Study design: Children with notified laboratory-confirmed (culture or PCR) pertussis disease were evaluated among the surveillance population of about 1 million infants, born between 1996 and 2007 and followed for pertussis disease from October 1997 to December 2007, for nearly 6 million person-years. Birth and vaccination dates of the diseased children are known from the surveillance programme. To estimate denominators of the age–dose–number-specific pertussis incidences, we used birth and vaccination dates from a vaccine trial with more than 72,000 infants combined with national pertussis vaccine coverage data for children in the surveillance population.
Results: For infants from 3 to <5 months of age, the incidence of pertussis disease with at least 14 days of cough decreased from 264/100,000 for unvaccinated infants to 155/100,000 for infants with one dose of a pertussis vaccine prior to onset of the disease. In the age range 5 to <12 months, the age–dose specific incidences were 526, 95, and 24/100,000 for infants with no, 1 and 2 doses, respectively. The rate of hospitalisation for infants with 1 dose of a pertussis vaccine prior to onset of the disease was significantly lower than for unvaccinated infants of the same age.

For many infants, there is a delay in administration of the vaccine doses according to the regular 3–5–12 month schedule (which has been the case for many years). Hypothetically, if all infants had been vaccinated exactly on schedule, we would expect about 28% fewer pertussis cases with at least 14 days of cough and 38% fewer hospitalisations due to pertussis, of cases possible to influence by vaccinations on schedule.
Conclusion: Pertussis vaccination had a significant effect among infants already after the first dose. This is particularly important for premature infants and infants with severe respiratory and cardiac diseases. A moderate decrease in the incidence of pertussis disease in infants and rate of hospitalisation could be expected if primary vaccinations were carried out closer to the scheduled time than is currently the practice in Sweden.

1. Introduction

Sweden was unique in radically changing the general pertussis childhood vaccination programme over time. After more than 20 years of use, the Swedish whole-cell pertussis (wP) vaccine was withdrawn in 1979 and there was no general vaccination against whooping cough for the following 17 years until 1996.

Since January 1996, two acellular pertussis (aP) vaccines have been used in the general childhood vaccination programme, at the ages of 3, 5 and 12 months, and the vaccine coverage has been in the same range, 98–99%, as the DT vaccine it replaced. From 1996 to 1998, a three-component DTaP vaccine was used in nearly all Swedish counties. It was replaced by a two-component DTaP vaccine in some counties in 1998 and 1999, and thereafter several

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switches, back and forth, have occurred between the two vaccines in different counties.

A pertussis surveillance programme was introduced in Sweden on 1 October 1997 to follow the burden and severity of pertussis disease over time among vaccinated, partly vaccinated and unvaccinated infants and young children born between 1996 and 2007. These children constitute the surveillance population of the current study [1–4].

During the non-pertussis vaccination years in Sweden, several pertussis vaccine studies were done [5–8]. The new vaccination programme against pertussis has thereafter, on the whole, been successful [1,2]. The overall incidence of laboratory-confirmed (i.e. culture or PCR positive) pertussis diseases in Sweden has reduced about 10-fold, from 121 to 150 per 100,000 years of follow-up during the non-vaccination period just before introduction of the new acellular vaccines, to 12–15 per 100,000 after 10 years of use of the DTaP vaccines [1,3]. It has dropped even further among infants and young children in the vaccinated birth cohorts. The highest age-specific incidences of pertussis disease in Sweden today are in infants 0–5 months of age. There were also indications of a reduced circulation of *Bordetella pertussis* [9].

Earlier results, comparing rates of hospitalisation among unvaccinated infants between 3 and 12 months of age with rates for infants vaccinated with one dose in the same age group, have indicated that some protection against severe disease might already be induced after the first dose of a DTaP vaccine [1]. We have also observed that several of the pertussis-diseased infants, unvaccinated or vaccinated, with only 1 or 2 doses before onset of the disease had not received their next scheduled pertussis vaccination on time.

The main aim of this study is to analyse 10 years of surveillance data to better understand the effect of 1 and 2 doses respectively of an acellular pertussis vaccine in younger age groups in comparison with unvaccinated and fully vaccinated children. Our hypothesis is that there is a dose–response association between the number of doses of a pertussis vaccine received before onset of the disease and the age-specific risk for pertussis disease. We will also study timeliness of the childhood immunisation programme, the vaccine coverage, and the effect of a delay in vaccination of the next scheduled dose among unvaccinated and infants vaccinated with only 1 or 2 doses before the pertussis episode.

To the best of our knowledge, our method of studying the protection of acellular pertussis vaccines in narrow age groups in infancy and early childhood and as a function of administered doses prior to disease has not been applied previously. It is therefore described in some detail in Section 2.

2. Materials and methods

2.1. End points and calculation of age–dose–number specific incidences

Two main end points for laboratory-confirmed (culture or PCR) pertussis disease have been studied taking age and number of doses of a pertussis vaccine at onset of the disease into account: (1) pertussis disease with at least 14 days of cough and (2) pertussis disease with hospitalisation for at least one night during the episode due to the disease. Risk for a pertussis disease according to the first end-point is defined as age-specific incidence, taking number of administered pertussis doses before onset of the disease into account. We call it an age–dose–number specific incidence.

Numerators for all incidence calculations were available from the pertussis surveillance programme. Three other data sources were used and combined to estimate the denominators.

1. Yearly census data for children in the surveillance population for calculation of the total number of follow-up years for the age intervals we wish to study (Table A1). The way annual census data are used for these calculations is described in detail in yearly reports [1],
2. Coverage data for children in the surveillance population and,
3. Birth and vaccination dates for infants from the large Swedish vaccine Trial II [5] used as a 'proxy' to lacking data for infants in the surveillance population. This study was performed in all Swedish local authorities except the Gothenburg area, covering about 90% of Swedish infants born between June 1993 and May 1994. More than 72,000 infants were recruited and received at least one dose of a pertussis vaccine according to the regular 3, 5 and 12 month vaccination schedule. In addition, about 10,000 infants in Trial II were vaccinated according to an experimental 2–4–6 month schedule. In practice the trial with DTP vaccine just replaced the ordinary DT vaccine administered at 3, 5 and 12 months from 1979. We have access to birth and vaccination dates in the vaccination register for all infants in this trial.

The last two data sources are used to estimate the percentage (the share in Table A1) of follow-up time with no, 1, 2 and 3 vaccine doses of a pertussis vaccine in the age intervals of follow-up for which we would like to calculate the age–dose–number-specific incidences. To calculate the denominators of the age–dose–number-specific incidences for children in the surveillance population, total number of person-years of follow-up for each age interval calculated in (1) was split by dose–number using the shares calculated in (2) and (3).

2.2. Pertussis surveillance data

The Swedish pertussis surveillance programme is based on an obligatory net-based reporting system (SMINET) in which all individuals in Sweden with a diagnosed pertussis disease are registered. Using telephone interviews of parents, clinical course data are collected for infants and children born in 1996 or later who had pertussis disease confirmed by culture or PCR. Vaccination dates are collected from child health centres (CHC) or school nurses. Data are used from "10 years" of follow-up for pertussis disease occurring after 1 October 1997 and before 31 December 2007, among children born between 1 January 1996 and 31 December 2007 in Sweden with the exception of the Gothenburg area [1].

2.3. Vaccine coverage data

Vaccine coverage data from all child health centres in Sweden are collected at the beginning of January each year. A coverage report includes data on all 2-year-old children enrolled at the CHC at that time: the number of children that have received only 1, only 2, or all 3 dose(s) of a pertussis vaccine, the number of unvaccinated children, and the number of children with unknown pertussis vaccination status are reported from each CHC and thereafter summarised at the Swedish Institute Communicable Disease Control (SMI) in a yearly report.

Pertussis vaccine coverage data for more than 600,000 children, collected from 2004 to 2009, for children born between 2001 and 2006 are used in this study. Variations year-by-year are negligible; data for the 6 years are summarised in Table 1. The table also includes the total number of 2-year-old children living in Sweden on 31 December added over the 6 years from 2003 to 2008 – i.e. these numbers are taken from the official census data by age valid only days before the coverage data collection in January.

We have used the coverage percentages for minor adjustments of the Trial II cohort of infants before calculation of shares