Effectiveness of 7-valent pneumococcal conjugate vaccine against radiologically diagnosed pneumonia in indigenous infants in Australia

KF O’Grady, JB Carlin, AB Chang, PJ Torzillo, TM Nolan, A Ruben & RM Andrews

Objective To evaluate the effectiveness of the 7-valent pneumococcal conjugate vaccine (PCV7) in preventing pneumonia, diagnosed radiologically according to World Health Organization (WHO) criteria, among indigenous infants in the Northern Territory of Australia.

Methods We conducted a historical cohort study of consecutive indigenous birth cohorts between 1 April 1998 and 28 February 2005. Children were followed up to 18 months of age. The PCV7 programme commenced on 1 June 2001. All chest X-rays taken within 3 days of any hospitalization were assessed. The primary endpoint was a first episode of WHO-defined pneumonia requiring hospitalization. Cox proportional hazards models were used to compare disease incidence.

Findings There were 526 pneumonia events among 10 600 children – an incidence of 3.3 per 1000 child-months; 183 episodes (34.8%) occurred before 5 months of age and 247 (47.0%) by 7 months. Of the children studied, 27% had received 3 doses of vaccine by 7 months of age. Hazard ratios for endpoint pneumonia were 1.01 for 1 versus 0 doses; 1.03 for 2 versus 0 doses; and 0.84 for 3 versus 0 doses.

Conclusion There was limited evidence that PCV7 reduced the incidence of radiologically confirmed pneumonia among Northern Territory indigenous infants, although there was a non-significant trend towards an effect after receipt of the third dose. These findings might be explained by lack of timely vaccination and/or occurrence of disease at an early age. Additionally, the relative contribution of vaccine-type pneumococcus to severe pneumonia in a setting where multiple other pathogens are prevalent may differ with respect to other settings where vaccine efficacy has been clearly established.

Introduction

Australian indigenous children suffer from extremely high rates of pneumonia and acute respiratory illness, and determining the potential for reducing disease burden with pneumococcal conjugate vaccines is therefore seen as a major health priority. In June 2001, the 7-valent pneumococcal conjugate vaccine (PCV7) was included in the Australian National Immunisation Program as part of a publicly funded course of primary vaccination at 2, 4 and 6 months of age, with a booster dose of the 23-valent polysaccharide pneumococcal vaccine at 18 months, for all indigenous children born on or after 1 April 2001. Catch-up campaigns were conducted in August 2001, targeting indigenous children aged up to 2 years in the northern region and up to 5 years in the central region of the Northern Territory.

Although antibiotic use in the community was high and the consequent yield of blood cultures at the time of hospitalization was poor, data from a central Australian study that used multiple diagnostic methods (culture and pneumolysin assays) had suggested that approximately 30% of hospitalized pneumonia cases were pneumococcal. PCV7 covered approximately 56% of pneumococcal serotypes causing invasive disease in indigenous children and 60% of pneumococcal serotypes carried in the nasopharynx (K Hare, Menzies School of Health Research, Darwin, personal communication, 2009) although the contribution of these serotypes to nonbacteraemic pneumonia was unknown. Assumptions based on these data suggested that a PCV7 uptake of at least 80% offered the potential for a 17% reduction of hospitalized pneumonia cases, an effect consistent with data from the pivotal trial of the vaccine in Californian children.

The aim of this study was to estimate the effectiveness of PCV7 in preventing radiologically diagnosed pneumonia as defined by the World Health Organization (WHO) among Northern Territory indigenous infants aged up to 18 months. The WHO case definition was chosen as it was the only one that could be standardized and systematically applied to the available data. For brevity, the term "pneumonia" will be used to refer to radiologically confirmed cases in the remainder of this paper.

Methods

Design

We conducted a historical cohort study of consecutive Northern Territory indigenous birth cohorts over an 8-year period.
Birth cohorts were constructed from two population-based health datasets – Northern Territory Immunisation Register data for the Northern Territory and Northern Territory hospital discharge data. The study was approved by the Human Research Ethics Committee of the Northern Territory Department of Health & Family Services and the Menzies School of Health Research (approval ID #05/49).

Setting
Of the Northern Territory’s 200,000 residents, 29% identify themselves as indigenous. Approximately 1500 births occur in this population per year. There are five public hospitals in the Northern Territory and one private hospital; the latter is rarely used by indigenous persons.

Health care is readily available in the Northern Territory. Indigenous infants present on average to primary health centres in remote areas at least once every two weeks in the first year of life. Most hospital admissions are to one of the five public hospitals. Out-of hospital deaths are rare in the Northern Territory. Mobility is predominantly limited to within regions in the Territory; interstate migration is infrequent.

All persons born in or who receive services at any public healthcare facility in the Northern Territory are allocated a unique health record number. This number is used for all subsequent episodes of medical care in the Territory, and it is the basis for registration on the Northern Territory Immunisation Register – a population-based register to which all vaccine providers report routinely. Children not born in a public hospital are added to the immunization register either through compulsory registration on the Northern Territory midwives’ data collection system or at the time of their first immunization encounter or first presentation for health care.

Population studied
Children were included if they were born between 1 April 1998 and 28 February 2005 and were resident in the Northern Territory at the time they were enrolled. Children were excluded if they died during the perinatal period (0–29 days of age) or while hospitalized if the admission date had been in the perinatal period, or if they had a first episode of pneumonia in the perinatal period.

Outcomes
All chest X-rays taken within the first 3 days of any admission for any diagnosis were obtained from all Northern Territory hospital radiology departments. Films were read independently by two general paediatricians or paediatric respiratory specialists blinded to all demographic, clinical and vaccination history data. Where readings were discordant, the films were read by a panel of paediatric radiologists similarly blinded to subject data and to the reason for discordance. All readers had achieved ≥80% agreement with the WHO training films before the start of the study, and inter-observer agreement during the study was ≥90%. The primary endpoint was a first episode of pneumonia (for consistency with clinical trials of the vaccine). Data on clinical presentation and laboratory investigations were not available for this study. For children in whom more than one chest X-ray was taken, any positive film classified the episode as a pneumonia event.

Person–time under observation commenced at 29 days of age (to exclude perinatal conditions) and ceased at the earliest of the following: date of admission for the first episode of pneumonia requiring hospitalization (failure date); 31 March 2005; date of death; date on which a child reached 18 months of age; or date on which a child received the 23-valent polysaccharide pneumococcal vaccine (to reduce confounding of PCV7 effects). Follow-up time was censored at 31 March 2005. As a result, not all children were followed until 18 months of age, particularly those in the last birth cohort.

Vaccination status
Vaccination status was assigned according to Northern Territory immunization record registers of PCV7 vaccination. As vaccination status varied with time, person–time was split and analysed by intervals of 0 doses of PCV7, 1 dose, 2 doses and 3 or more doses. To allow sufficient time for an adequate immune response, a dose was not considered to have been received until 14 days after actual administration.

Covariates
Data available on the children in the study were limited to demographic information, vaccination history and hospitalization data; only age, sex and region of residence could be included as covariates in the analyses. Age was considered a time-varying covariate categorized into 3-month age groups (0 to < 3 months, 3 to < 6 months, 6 to < 9 months, 9 to < 12 months, 12 to < 15 months, 15 to < 18 months).

To assess the potential for differential vaccination of children with key co-morbidities known to be associated with the risk of pneumonia (gastroenteritis, anaemia and/or malnutrition), we assessed the differences in vaccination status between hospitalized children with and without these conditions. To account for opportunity for exposure to 3 doses of vaccine, this analysis was conducted only for children born on or after 1 April 2001 who were 7 months of age or older at the time of admission.

Sample size
This study was nested within a larger burden of pneumonia study conducted in the Northern Territory over the same time period. On the basis of data from central Australia and taking into account differences in the invasive pneumococcal disease burden between Northern Territory regions, we assumed an incidence of 70 cases per 1000 population per year across the Territory as a whole. If 80% coverage is assumed (on the basis of routine childhood immunization data), 3 birth cohort years before and after the vaccine would provide 80% power (0.05) to detect a 20% reduction in pneumonia incidence.

Statistical analyses
Crude incidence rates were calculated by dividing number of cases by person–time at risk and are presented in units per 1000 child–months with corresponding 95% confidence intervals (CIs). Cox proportional hazards models with time-varying covariates were used to evaluate the association between receipt of PCV7 (categorized as 0, 1, 2 or 3 doses) and the time
to first pneumonia event. Vaccine effectiveness (VE) was calculated from the estimated hazard ratio (HR) for 1, 2 and 3 doses compared to zero [VE = (1−HR) × 100].

Potential predictors evaluated in the models were age, sex, birth cohort and region of residence. Schoenfeld residual tests were used to evaluate the proportional hazards assumption for each covariate. Likelihood ratio tests were used to assess covariate effects and potential interactions. Data were analysed using Stata SE v9.1 (StataCorp, College Station, Texas, United States of America).

The primary analysis evaluated the association between vaccination and pneumonia in children born on or after 1 April 1998; children born before 1 April 2001 were included as historical controls. Secondary analyses were performed including only children born on or after 1 April 2001 and with the observation period commencing at 5 months, by which time children should have received 2 doses of vaccine.

Results

A total of 10 600 children were included in the final analysis. There was no evidence of a change in all-cause hospitalization rates over time (average incidence: 66.0 per 1000 child–months, 95% CI: 64.1–68.0) or the chest X-ray rate per 1000 hospitalizations. A total of 8488 chest X-rays were taken within 3 days of admission in 6775 episodes of care. Chest X-rays were considered of inadequate quality for endpoint diagnosis in 984 (14.5%) episodes. In this analysis, these episodes were considered negative for the study endpoint.

There were 526 first episodes of pneumonia – an overall incidence of 3.3 per 1000 child–months (95% CI: 3.1–3.6). Although the data were suggestive of a declining incidence over time (average incidence: 66.0 per 1000 child–months, 95% CI: 64.1–68.0) or the chest X-ray rate per 1000 hospitalizations. A total of 8488 chest X-rays were taken within 3 days of admission in 6775 episodes of care. Chest X-rays were considered of inadequate quality for endpoint diagnosis in 984 (14.5%) episodes. In this analysis, these episodes were considered negative for the study endpoint.

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of an effect in older children.17 However, the WHO definition was not used in the latter two studies and their findings therefore cannot be readily compared to ours.

Possible explanations for the differences between our results and those reported in the clinical trials include: chance variation (our 95% CI allows the possibility of moderately substantial benefit after 3 doses), differences in case ascertainment methods, differences in vaccine schedules and serotype coverage, the possibility that the seven Streptococcus pneumoniae vaccine serotypes are not responsible for the majority of severe pneumonia in these children and/or serotype replacement. The latter may be of particular relevance given that nasopharyngeal carriage of the serotypes targeted by the PCV7 has declined dramatically since its introduction in the Northern Territory, overall carriage of all serotypes remains unchanged.18 Similarly, rates of pneumonia due to respiratory syncytial virus and influenza virus in this population are high.5,19,20 While there are no data on its contribution to lower respiratory infection in these children, carriage of non-encapsulated Haemophilus influenzae is as high as 100% by 120 days of age.21 Half of the cases in our study occurred before 7 months of age and one quarter before 3 months of age. These data are consistent with the known early colonization by respiratory pathogens (e.g. Moraxella catarrhalis, H. influenzae and S. pneumoniae) in these children.26,27 It is clear that an effective vaccine would need to be given earlier to Australian indigenous children in order to achieve any substantial effect at the population level.

In older children aged 6 months or more, timeliness of vaccination is

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**Table 1. Incidence of WHO-defined consolidated pneumonia, by birth cohort and number of vaccine doses received, among NT-resident Australian indigenous children aged 29 days to 18 months, 1998–2005**

<table>
<thead>
<tr>
<th></th>
<th>Cohort</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Apr 98–Mar 99</td>
<td>Apr 99–Mar 00</td>
</tr>
<tr>
<td>0 doses</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cases</td>
<td>89</td>
<td>84</td>
</tr>
<tr>
<td>Child–months</td>
<td>22 514.3</td>
<td>24 312.7</td>
</tr>
<tr>
<td>Incidence* (95% CI)</td>
<td>3.95</td>
<td>3.46</td>
</tr>
</tbody>
</table>

(3.21–4.87) (2.79–4.28) (2.39–3.99) (2.20–5.08) (2.79–6.55) (1.83–5.42) (0.66–4.66) (3.10–3.91)

| 1 dose   |        |       |       |       |       |       |       |       |
| Cases    | NA     | 0     | 8     | 28    | 15    | 17    | 7     | 75    |
| Child–months | 65.9 | 3 047.2 | 4 653.3 | 4 658.5 | 4 444.5 | 2 211.4 | 19 080.8 |
| Incidence* (95% CI) | NA     | 0     | 2.63  | 6.02  | 3.22  | 3.82  | 3.17  | 3.93  |

(1.31–5.25) (4.15–8.71) (1.94–5.34) (2.38–6.15) (1.51–6.64) (3.13–4.93)

| 2 doses  |        |       |       |       |       |       |       |       |
| Cases    | NA     | 0     | 12    | 11    | 23    | 13    | 3     | 62    |
| Child–months | 1.6 | 2 918.3 | 4 653.4 | 4 630.7 | 4 232.8 | 1 386.0 | 17 822.7 |
| Incidence* (95% CI) | NA     | 0     | 4.11  | 2.36  | 4.97  | 3.07  | 2.16  | 3.47  |

(2.34–7.24) (1.31–4.27) (3.30–7.47) (1.78–5.29) (0.69–6.71) (2.71–4.46)

| 3 doses  |        |       |       |       |       |       |       |       |
| Cases    | NA     | NA    | 1     | 25    | 37    | 32    | 3     | 98    |
| Child–months | NA | 883.9 | 11 713.9 | 12 401.8 | 11 134.9 | 1 176.1 | 37 310.6 |
| Incidence* (95% CI) | NA     | NA    | 1.13  | 2.13  | 2.98  | 2.87  | 2.55  | 2.63  |

(0.16–8.03) (1.44–3.16) (2.16–4.12) (2.03–4.06) (0.82–7.90) (2.15–3.20)

| Total    |        |       |       |       |       |       |       |       |
| Cases    | 89     | 84    | 58    | 22    | 21    | 13    | 4     | 291   |
| Child–months | 22 514.3 | 24 380.2 | 25 629.0 | 27 592.2 | 26 607.0 | 23 941.9 | 7 061.5 | 15 7726.1 |
| Incidence* (95% CI) | 3.95 | 3.46 | 3.08 | 3.12 | 3.61 | 3.13 | 2.41 | 3.33 |

(3.21–4.87) (2.78–4.27) (2.47–3.84) (2.52–3.85) (2.95–4.41) (2.50–3.93) (1.49–3.87) (3.06–3.63)

* Cases per 1000 child-months.
We were able to commence measure-
potential variations in risk over time.
time intervals and accounted for the
pneumonia as children aged over small
methods allowed an assessment of
cination history.
subject’s demographic, clinical and vac-
and the person analysing the data was
son collected and processed all X-rays,
during the study period. The same per-
enous infant in the Northern Territory
that we reviewed every hospitalization
5 months and older.

The major strength of this study is
we reviewed every hospitalization and
every chest X-ray for every indig-
which children enter a study may lead
to differences in risk profiles between
children. This would be critical in studies without randomization of
children to different groups. Account-
ing for the risk of infection and subse-
disease early in life is critical to the
formulation of policies concerning
schedules and number of doses
required by specific ages.

We were able to exclude infants who
who had suffered a first episode of
WHO-defined consolidated pneu-
in the perinatal period and who
were therefore likely to have a different
profile from those who had sur-
vived this period without contracting
Importantly, as individual
not required for entry into the
we were able to include every
Northern Territory child. A major issue
in clinical trials and other studies that
enrol individuals is accounting for
important differences between those who do and do not consent to
participate. Similarly, generally only
children are eligible for inclu-
clinical trials.

Uncertainty about the accuracy of
person–time denominator is a limita-
tion. However, increasing vaccination
coverage as children aged suggested that
children were continuing to present
to Northern Territory health services
throughout infancy. The predominant
reasons for censoring in this study were
subjects reaching 18 months of age
and the study reaching its end date of
31 March 2005. Both of these are ad-
ministrative censoring points and the
bias to the study is less important given
that this type of censoring is largely
independent of the characteristics of
the individuals under observation.29
However, the considerably shorter
person–time available in the analysis

likely to be critical. While coverage
reached over 85% by 18 months of
,28 fewer than 40% of eligible chil-
ders had received 3 doses of the vac-
by 7 months of age. The necessity of
3 doses in infancy is suggested by this
study’s data: while not statistically
significant, the data indicated a reduction
incidence of 24% (95% CI: −9–47)
after the third dose in children aged
months and older.

The study design and analysis
methods allowed an assessment of
pneumonia as children aged over small
time intervals and accounted for the
potential variations in risk over time.
We were able to commence measure-
ment of person–time at risk at the same
time for all individuals (29 days). In
populations with rapid acquisition and
nasopharyngeal colonization of respira-
tory pathogens early in life, as occurs
in the Northern Territory indigenous
population,26 variations in the age at
which children enter a study may lead
to differences in risk profiles between
these children. This would be critical in studies without randomization of
children to different groups. Account-
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However, the considerably shorter
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\[ \text{Table 2. Incidence of WHO-defined consolidated pneumonia, by age group, among NT-resident Australian indigenous children aged 29 days to 18 months, 1998–2005} \]

<table>
<thead>
<tr>
<th>Age group</th>
<th>No. children</th>
<th>Cases</th>
<th>Child–months</th>
<th>Incidence (^a) (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>29 days to &lt; 3 months</td>
<td>10 600</td>
<td>128</td>
<td>30 596.2</td>
<td>4.18 (3.52–4.97)</td>
</tr>
<tr>
<td>3 to &lt; 6 months</td>
<td>10 102</td>
<td>112</td>
<td>29 210.2</td>
<td>3.83 (3.19–4.61)</td>
</tr>
<tr>
<td>6 to &lt; 9 months</td>
<td>9 668</td>
<td>95</td>
<td>27 921.7</td>
<td>3.40 (2.78–4.16)</td>
</tr>
<tr>
<td>9 to &lt; 12 months</td>
<td>9 225</td>
<td>80</td>
<td>26 625.1</td>
<td>3.00 (2.41–3.74)</td>
</tr>
<tr>
<td>12 to &lt; 15 months</td>
<td>8 766</td>
<td>74</td>
<td>25 186.2</td>
<td>2.93 (2.34–3.69)</td>
</tr>
<tr>
<td>15 to &lt; 18 months</td>
<td>8 275</td>
<td>37</td>
<td>18 186.6</td>
<td>2.03 (1.47–2.81)</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>10 600</strong></td>
<td><strong>526</strong></td>
<td><strong>157 726.1</strong></td>
<td><strong>3.33 (3.06–3.63)</strong></td>
</tr>
</tbody>
</table>

\(^a\) Cases per 1000 child–months.

\[ \text{Table 3. Age-adjusted hazard rate ratios for WHO-defined consolidated pneumonia in vaccinated and unvaccinated NT indigenous infants aged 29 days to 18 months, by number of vaccine doses and analysis time period} \]

<table>
<thead>
<tr>
<th>Time period and cohort</th>
<th>0 doses</th>
<th>1 dose</th>
<th>2 doses</th>
<th>3 doses</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Cases (child–months)</td>
<td>Cases (child–months)</td>
<td>HRR</td>
<td>95% CI</td>
</tr>
<tr>
<td>Children born 1 Apr 2001 – 28 Feb 2005, from 29 days of age</td>
<td>61 (17 909)</td>
<td>68 (15 972)</td>
<td>1.02</td>
<td>0.69–1.49</td>
</tr>
<tr>
<td>Children born 1 Apr 1998 – 28 Feb 2005, from 29 days of age</td>
<td>295 (83 623)</td>
<td>276 (19 085)</td>
<td>1.01</td>
<td>0.78–1.32</td>
</tr>
<tr>
<td>All children, from 5 months of age (^a)</td>
<td>155 (49 362)</td>
<td>21 (7 709)</td>
<td>0.83</td>
<td>0.52–1.32</td>
</tr>
</tbody>
</table>

\(^a\) Excludes 183 children who were censored before reaching 5 months of age.
for the last birth cohort may have limited the study's ability to detect vaccine effects. This is of particular relevance to interpreting the trend observed over time, as it is impossible to determine whether the decline in rates observed in the last year was sustained or was just a yearly variation in the incidence of disease. Moreover, declines appeared to be occurring independent of vaccination status. This underscores the need for ongoing surveillance of severe pneumonia in the Northern Territory population.

The lack of information on potentially confounding factors – particularly known risk factors such as prematurity, low birth weight, co-morbidities and exposure to household tobacco smoke – necessitates a cautious approach to the interpretation of vaccine effectiveness in this study. Differences in these factors between vaccinated and unvaccinated children could have confounded the vaccine effectiveness. However, for these factors to explain our findings, vaccinated children would need to be at higher risk of exposure. Our data do suggest that vaccination status did not differ between hospitalized children with and without the other major causes of paediatric morbidity in the Northern Territory (gastroenteritis, malnutrition and anaemia).

A final limitation is the potential lack of power in this study to demonstrate an effect. Baseline disease incidence was calculated on estimates derived from a study that did not use the WHO definition for radiologically confirmed pneumonia because it was not available at the time. Because of our use of the WHO definition and our decision to evaluate only the first episode, disease incidence in this population was considerably lower than anticipated. Additional analyses evaluating repeated episodes of WHO-defined radiologically diagnosed pneumonia and all-cause acute lower respiratory infection and pneumonia requiring hospitalization have been performed for children from 5 to 23 months of age and have not changed our findings substantially.

We were unable to demonstrate definitively that PCV7 had an effect in preventing a first episode of radiologically diagnosed pneumonia in a setting characterized by high rates occurring very early in infancy with delays in delivery of the primary vaccination series. This study highlights the importance of immunization timeliness to extrapolating the results of vaccine efficacy established in randomized controlled trials relative to vaccine effectiveness at the population level with vaccine delivery under routine field conditions. Optimizing the timeliness of vaccination in the Northern Territory infant population is a priority public health measure. Ongoing surveillance and further studies are required to evaluate whether the trend observed in the final year of the study was maintained.

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Résumé

Efficacité du vaccin antipneumococcique conjugué heptavalent contre la pneumonie diagnostiquée par examen radiologique chez les nourrissons indigènes en Australie

Objectif Évaluer l’efficacité du vaccin antipneumococcique conjugué heptavalent (PCV7) dans la prévention de la pneumonie diagnostiquée par examen radiologique selon les critères de l’Organisation mondiale de la Santé (OMS) chez les nourrissons indigènes du Territoire du Nord en Australie.


Résultats Nous avons relevé 526 cas de pneumonie parmi 10600 enfants - soit une incidence de 3,3 cas pour 1000 enfants-mois ; 183 épisodes (34,8 %) sont intervenus avant l’âge de 5 mois et 247 (47,0 %) à 7 mois. Parmi les enfants étudiés, 27 % avaient reçu 3 doses de vaccin à l’âge de 7 mois. Les rapports de risques pour le critère de jugement pneumonie valaient 1,01 pour la comparaison 1 dose de vaccin contre 0 dose ; 1,03 pour la comparaison 2 doses contre 0 dose ; et 0,84 pour la comparaison 3 doses contre 0 dose.

Conclusion Les preuves d’une réduction par le vaccin PCV7 de l’incidence de la pneumonie diagnostiquée par examen radiologique chez les nourrissons indigènes du territoire du Nord étaient limitées, malgré la présence d’une tendance non significative à la manifestation d’un effet après l’administration de la troisième dose. Ces résultats peuvent s’expliquer par la fréquence des retards dans la vaccination et/ou par l’apparition de la maladie à un âge précoce. De plus, la contribution des germes pneumococciques de type vaccinal à la pneumonie sévère dans un contexte où l’on rencontre de nombreux autres agents pathogènes peut être différente de leur contribution dans une situation où l’efficacité du vaccin a été clairement établie.

Resumen

Eficacia de la vacuna antineumocócica conjugada heptavalente contra la neumonía diagnosticada radiológicamente en lactantes indígenas en Australia

Objetivo Determinar la eficacia de la vacuna antineumocócica conjugada heptavalente (PCV7) en la prevención de la neumonía diagnosticada radiológicamente de acuerdo con los criterios de la Organización Mundial de la Salud (OMS) entre lactantes indígenas del Territorio Septentrional de Australia.

Métodos Realizamos un estudio de cohorte histórica con cohortes de nacimiento de indígenas consecutivas entre el 1 de abril de 1998 y el 26 de agosto de 2005. Los niños fueron sometidos a seguimiento hasta los 18 meses de edad. El programa de administración de PCV7 comenzó el 1 de junio de 2001. Se estudiaron todas las radiografías de tórax realizadas dentro de los tres primeros días de hospitalización. La variable de evaluación principal fue un primer episodio de neumonía acorde con la definición de la OMS que requiriese hospitalización. Para comparar la incidencia de la enfermedad se usaron modelos de riesgos proporcionales de Cox.

Resultados Se registraron 526 eventos de neumonía entre 10 600 niños, lo que supone una incidencia de 3,3 por 1000 niños-mes; 183 episodios (34,8%) se produjeron antes de los 5 meses de edad, y 247 (47,0%) antes de los 7 meses. De los niños estudiados, un 27% habían recibido 3 dosis de vacuna antes de los 7 meses de edad. Los cocientes de riesgos instantáneos para la neumonía como variable de evaluación fueron de 1,01 para 1 frente a 0 dosis; 1,03 para 2 frente a 0 dosis; y 0,84 para 3 frente a 0 dosis.

Conclusion Los datos obtenidos no parecen respaldar la idea de que la PCV7 reduzca la incidencia de neumonía confirmada radiológicamente entre los lactantes indígenas del Territorio Septentrional, pese a que se detecta una tendencia, no significativa, a la manifestación de un efecto después de la tercera dosis. Estos resultados podrían explicarse suponiendo que la vacunación no se hizo en su debido momento y/o la enfermedad apareció a una edad temprana. Además, la contribución relativa del neumococo del tipo vacunal a la neumonía grave en un entorno donde concurren con frecuencia muchos otros agentes patógenos puede diferir respecto a otros entornos en que la eficacia de la vacuna ha quedado claramente demostrada.

References