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Original Article

The distribution and annual changes in the *Streptococcus pneumoniae* serotypes in adult Japanese patients with pneumococcal pneumonia from 2011 to 2015

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ABSTRACT

Background: We previously reported a decrease in the vaccine serotypes of a 7-valent pneumococcal conjugate vaccine (PCV7) and pneumococcal polysaccharide vaccine (PPSV) 23 in adult pneumonia patients after starting PCV7 vaccination in children in Japan between 2011 and 2013, suggesting that the vaccination of children had an indirect effect on adults. PCV7 was replaced by PCV13 in 2013 and was authorized for individuals ≥65 in 2014; vaccination with PPSV23 has been routinely implemented since the same year. We continuously evaluated the pneumococcal serotype changes.

Methods: This retrospective epidemiological study was performed at the University of Occupational and Environmental Health, Japan, from January 2014 to December 2015, while also referring to the data from January 2011 to December 2013. The pneumococcal serotypes that were isolated from pneumonia patients and clinical information were evaluated.

Results: The proportions of the PCV7 and PCV13 vaccine serotypes significantly decreased each year (from 2011 to 2015) from 46.4% to 8.3% ($p < 0.05$) and 71.4% to 33.3% ($p < 0.05$), respectively. The PPSV23 serotypes without PCV13 showed a continuous, mild increase, while the mortality rates tended to decrease in patients with pneumococcal pneumonia.

Discussion: The present study showed that the vaccine serotypes of PCV7 and PCV13 have been decreasing since the introduction of PCV7 in October 2009 and since PCV13 was introduced to replace PCV7 from November 2013, and that the mortality rates of patients have tended to decrease. These results indicate that a continuous analysis of the pneumococcal serotype data is necessary for the appropriate administration of vaccines.

1. Introduction

The proportion of children with invasive pneumococcal disease (IPD) in the United States (US) decreased drastically following the introduction, in 2000, of the 7-valent pneumococcal conjugate vaccine (PCV7) for all children of 2–23 months of age and children of 24–59 months of age who are at risk of pneumococcal infection [1,2]. In addition to the decrease in the rates of IPD in children, the proportion of adult IPD patients with the PCV7 serotypes also decreased in the US [1,3–5]. This phenomenon was explained by the indirect suppressive effect of PCV7 vaccination in children on adult IPD.

Similar trends have been observed in Japan after since PCV7 vaccination was introduced for children in 2009, with a decrease in the rates of childhood IPD [6], and a decrease in the proportion of PCV7 serotypes in adult IPD patients [7]. We previously reported the changes in the pneumococcal serotypes in Japan between 2011 and 2013, after PCV7 vaccination in children, and found a decrease in the vaccine serotypes of PCV7 and the 23-valent pneumococcal

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polysaccharide vaccine (PPSV23), suggesting that the vaccination of children had an indirect effect on adults [8].

With regard to PCV13, PCV13 vaccination in children was reported to indirectly lead to serotype replacement in adult IPD patients in the US, where the percentage of PCV13 serotypes was reduced in non-IPD patients [9,10]. In Japan, PCV7 was replaced with PCV13 in November 2013 for the vaccination of children, and PCV13 was subsequently authorized for use in adults of ≥65 years of age in June 2014. Furthermore, the amount of public support provided for routine vaccination with PPSV23 for healthy people of ≥65 years of age increased in Japan from October 2014.

In the present study, we continuously evaluated the changes in the pneumococcal serotypes of adult patients with pneumonia, and analyzed the influence of PPSV23 vaccination and the replacement of PCV7 with PCV13 vaccination in Japan in 2014 and 2015.

2. Patients and methods

This retrospective observational study was performed at the University of Occupational and Environmental Health, Japan from January 2014 to December 2015, with additional reference to data from January 2011 to December 2013 [8]. Similarly to a previous report that included 81 patients and 89 episodes [8], the present study included a total of 74 patients and 82 episodes (2014, 44 patients [46 episodes]; 2015, 28 patients [36 episodes]) of pneumococcal pneumonia from patients whose respiratory cultures were positive for *Streptococcus pneumoniae*.

The evaluated items, the diagnostic criteria of community-acquired pneumonia (CAP), healthcare-associated pneumonia (HCAP) and hospital-acquired pneumonia (HAP), the culture methods, the evaluation of the minimum inhibitory concentration (MIC) and the evaluation of the pneumococcal serotypes were similar to our previous report [8]. The research protocols of the present study complied with the Declaration of Helsinki and were approved by the ethics committee of the University of Occupational and Environmental Health, Japan (No. 26–226). This study did not require written informed because it was retrospective in nature and contained no personal information.

The statistical analyses were performed using the SPSS software program (version 19; SPSS Inc.; Chicago, IL, USA). Fisher's exact test for tables (2 × 2) and the Mann–Whitney (non-parametric) test were applied, as appropriate. p Values of <0.05 were considered to indicate statistical significance.

3. Results

3.1. Patient characteristics

Table 1 shows the background characteristics of the patients with pneumococcal pneumonia. The average age was 67.7 ± 14.0 years, 60.2% of the patients were male, and the average body mass index (BMI) was 22.1 ± 18.6. One hundred thirteen *S. pneumoniae* isolates were collected from patient sputum samples (66.1%), and 25 (14.6%)/13 (7.6%)/20 (11.7%) were collected via intratracheal tube suction/intrabronchial sampling/bronchoalveolar lavage (BALF), respectively. The numbers (percentages) of patients with CAP/HCAP/HAP/IPD were 90/34/47/7 (52.6%/19.9%/27.5%/0.6%), respectively. Seventeen (9.9%) patients had a history of PPSV23 vaccination (the numbers of serotype 3/15A/unknown were 4/2/2, respectively; the others included one case each of 6A, 6D, 10A, 19A, 22F, 23A, 24F, 34 and 35B); 135 (78.9%) had no history of PPSV23 vaccination. The vaccination status of 19 (11.1%) patients was unknown. The numbers (percentages) of patients with a premorbid European Cooperative Oncology Group-Performance Status (ECOG-PS) of 0–1/2/3–4 were 102/19/50 (59.6%/11.1%/29.2%), respectively. Table 2 shows the clinical and laboratory data, the Pneumonia Severity Index (PSI), and the rates of mortality and drug resistance. The numbers of positive/negative/unknown urinary antigen tests for *S. pneumoniae* were 41/43/87 (24.0%/25.1%/50.9%), and the average PSI score was 102.1 ± 40.2. The in-hospital mortality rate was 8.5% (12 patients). Antibiotic susceptibility testing showed that the numbers of patients with penicillin-resistant *S. pneumoniae* (PRSP)/macrolide-/quinolone-resistant pneumococci were 0/141/4 (0.0%/82.5%/2.3%), respectively.

Table 1
Characteristic of patients with pneumococcal pneumonia.

Viables	Total (n = 171)
Age, years, mean ± SD	67.7 (14.0)
Gender, male; n (%)	103 (60.2)
Sample type; n (%)	
Sputum	113 (66.1)
Intratracheal tube suction	25 (14.6)
Intrabronchial sampling	13 (7.6)
BALF	20 (11.7)
Type of pneumonia; n (%)	
CAP	90 (52.6)
HCAP	34 (19.9)
HAP	47 (27.5)
IPD; n (%)	7 (0.6)
Histories of use of PPSV23; n (%)	
Received	17 (9.9)
Not received	135 (78.9)
Unknown	19 (11.1)
BMI, mean ± SD[a]	22.1 (18.6)
Smoking; n, (%)[b]	
Smoker	26 (16.7)
Ex-smoker	59 (37.8)
Nonsmoker	71 (45.5)
B.I, mean ± SD[c]	417.6 (537.7)
ECOG PS of premorbid condition, median (IQR)	1 (1.5)
0–1; n (%)	102 (59.6)
2; n (%)	19 (11.1)
3–4; n (%)	50 (29.2)
Comorbidity; n, (%)	
Chronic respiratory disease	26 (15.2)
COPD	17 (9.9)
Bronchiectasis	8 (4.7)
Lung cancer	17 (9.9)
Interstitial pneumonia	11 (6.4)
Cerebrovascular disease	41 (24.0)
Neuromuscular disease	20 (11.7)
Dementia	13 (7.6)
Pharyngeal disorder	12 (7.0)
Gastroesophageal disorder	5 (2.9)
Diabetes mellitus	39 (22.8)
Malignancy excluding lung cancer	28 (16.4)
Congestive heart failure	17 (9.9)
Chronic kidney disease	12 (7.0)
Chronic liver disease	11 (6.4)
RA or Sjogren's syndrome	7 (4.1)
Collagen disease	11 (6.4)
Psychiatric disease	9 (5.3)
Sleeping medications	15 (8.8)
Glucocorticoids (PSL ≥5 mg/day)	26 (15.2)
Immunosuppressive agent	17 (9.9)

Definition of abbreviations: SD: standard deviation, BALF: bronchoalveolar lavage fluid, CAP: community-acquired pneumonia, HCAP: healthcare-associated pneumonia, HAP: hospital-acquired pneumonia, PPSV23: 23-valent pneumococcal polysaccharide vaccine, IPD: invasive pneumococcal diseases, BMI: body mass index, ECOG PS: Eastern Cooperative Oncology Group performance status, BI: brinkman index, COPD: chronic obstructive pulmonary disease, RA: rheumatoid arthritis, PSL: prednisolone.

[a] BMI was evaluated in 143 patients.

[b] Smoking was evaluated in 156 patients.

[c] B.I was evaluated in 153 patients.