

Effectiveness of a 23-valent Pneumococcal Polysaccharide Vaccine for the Prevention of Pneumococcal Pneumonia in the Elderly with Chronic Respiratory Diseases: A Case-control Study of a Single Center

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Abstract

Background: The effectiveness of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) in preventing non-invasive pneumococcal pneumonia (non-IPD) has been controversial.

Methods: To evaluate the effectiveness of the PPSV23 in elderly outpatients with chronic respiratory diseases, we carried out a case-control study, including 4128 outpatients aged ≥ 65 years, in the respiratory department.

Results: There were 320 vaccinated patients, of which 164 were diagnosed with pneumococcal pneumonia. The adjusted odds ratio was 0.39 (95 % confidence interval (CI), 0.17 to 0.89). In the subsets consisting of age groups ≥ 70 and ≥ 75 years, the adjusted odds ratio (95 % CI) was respectively 0.16 (0.04 to 0.67) and 0.15 (0.02 to 1.12).

Conclusion: This real-world study suggests that PPSV23 is effective in preventing pneumococcal pneumonia in the elderly with chronic respiratory diseases and in the older population (age ≥ 75 years).

Background

Streptococcus pneumoniae can cause pneumonia and invasive pneumococcal diseases (IPDs), which result in considerable morbidity and mortality worldwide [1, 2]. The Advisory Committee on Immunization Practices recommends the use of the 23-valent pneumococcal polysaccharide vaccine (PPSV23) or the 13-pneumococcal conjugate vaccine for all the elderly (age ≥ 65 years) and for immunocompromised adults [3]. Although the effectiveness of the PPSV23 in preventing IPD has been reported, its effectiveness in preventing non-invasive pneumococcal pneumonia (non-IPD) has been inconsistent [4–6]. Some researchers have targeted both healthy individuals and patients with various diseases at nursing home residences [5, 7].

We hypothesized that the PPSV23 would be useful in preventing pneumococcal pneumonia in elderly outpatients with chronic respiratory diseases. This study aimed to assess the effectiveness of the PPSV23 among elderly outpatients in clinical practice.

Methods

Study design and population

This study was a retrospective case-control design. The target population was defined as outpatients aged ≥ 65 years, with chronic respiratory diseases, treated between 2015 and 2017 in the respiratory department of Shizuoka General Hospital. From this sample, the case and control groups consisted of patients with and without pneumococcal pneumonia, respectively.

Diagnosis of non-invasive pneumococcal pneumonia

Respiratory physicians diagnosed pneumonia based on clinical findings such as fever, hypothermia, chills, cough, sputum production, pleuritic chest pain, fatigue, tachypnea, white blood cell count > 9300 , or < 4000 cells/mm³, and new pulmonary infiltrates on chest radiography [2]. In this study, all patients with pneumonia met these criteria. Non-IPD was diagnosed based on the positive results of urine pneumococcal antigen and sputum culture, but a negative blood culture for pneumococcus.

Definitions

The chronic respiratory diseases in this study included lung cancer, asthma, chronic obstructive pulmonary disease (COPD), interstitial pneumonia, pulmonary non-tuberculous mycobacteriosis (NTM), pulmonary tuberculosis, and others. The history of PPSV23 vaccination was obtained from medical records and declarations by patients or their families. Patients were considered vaccinated when they had received the PPSV23 within five years prior to the diagnosis of pneumonia. Patients without medical records or whose families had no knowledge of their vaccination statuses were considered unvaccinated.

Statistical analysis

The chi-squared tests for categorical variables and t-tests for continuous variables were used in comparing both groups. To evaluate the effectiveness of the PPSV23, we performed a logistic regression analysis, and then the odds ratio (OR), 95 % confidence interval (CI), and p-value (based on Wald test) were calculated. The adjusted OR was estimated by the quantile stratification method of propensity scores. The propensity score was estimated using multivariate logistic regression models with potential confounders as covariates, which included all variables of table 1. We also made two subsets: those ≥ 70 years, and ≥ 75 years, and compared their adjusted ORs with that in all patients. As a sensitivity analysis, we estimated double-robust adjusted OR in case-control studies under causal inference [8], and we confirmed whether the point estimation of OR, as mentioned above, was overestimating the effect. A p-value of < 0.05 was considered to be statistically significant. Statistical analyses were performed using SAS version 9.4 (SAS Institute, Cary, NC, USA).

Results

Patients background

Between January 1, 2015, and December 31, 2017, 4218 outpatients aged ≥ 65 years with chronic respiratory diseases visited our department. The patient flow is shown in Fig. 1. A total of 320 patients received the PPSV23, while 3898 did not. Of the 320 vaccinated patients, 6 developed pneumococcal pneumonia, compared to 158 of the 3 898 unvaccinated patients.

The baseline characteristics of the case and control group on January 1, 2015, are shown in Table 1. Patients in the case group were more current-smokers, as well as had other chronic respiratory diseases,

diabetes, chronic heart disease, and had higher use of systemic corticosteroids, than the control group. The number of patients in the case group with lung cancer was less than that of the control group.

Table 1
Characteristics of patients with and without pneumococcal pneumonia.

Variable and category (reference)	Case group (n=164)	Control group (n=4,054)	P-value
Age, y*	76.2 ± 7.3	75.1 ± 6.7	0.127
65-69	32 (19.5)	984 (24.3)	0.153
70-74	44 (26.8)	1,098 (27.1)	
75-79	36 (22.0)	950 (23.4)	
80+	56 (34.1)	1,063 (26.2)	
Male (vs. female)	113 (68.9)	2,525 (62.3)	
Current (reference: ex-smokers)	108 (65.9)	2,068 (51.0)	0.001
Chronic respiratory diseases (vs. absent)			
Asthma	30 (18.3)	685 (16.9)	0.671
COPD	42 (25.6)	959 (23.6)	0.574
Lung cancer	45 (27.4)	1,594 (39.3)	0.002
Interstitial pneumonia	29 (17.7)	703 (17.3)	0.916
NTM	10 (6.1)	449 (11.1)	0.054
Others [†]	48 (29.3)	746 (18.4)	0.001
Diabetes (vs. absent)	65 (39.6)	1,209 (29.8)	0.023
Chronic heart disease (vs. absent)	95 (57.9)	1,891 (46.6)	0.005
Chronic kidney disease (vs. absent)	13 (7.9)	299 (7.4)	0.761
Systemic corticosteroid user (vs. absent)	65 (39.6)	1,189 (29.3)	0.007
Values are expressed as numbers and proportions in parentheses.			
*Mean ± SD.			
[†] Other chronic respiratory diseases included chronic pulmonary aspergillosis, old pulmonary tuberculosis, sarcoidosis, and chronic cough.			
COPD: chronic obstructive pulmonary disease, NTM: non-tuberculous mycobacteriosis.			

Effectiveness of the vaccine against pneumococcal pneumonia

Pneumococcal pneumonia prevention crude OR (95 % CI) was 0.45 (0.20-1.03, $p = 0.059$), and the adjusted OR was 0.39 (0.17-0.89) (Fig. 2). There was a trend towards lower OR in older patients: higher OR (95 % CI) in ≥ 65 years, 0.16 (0.04-0.67) in subset 1 (≥ 70 years), and 0.15 (0.02-1.12) in subset 2 (≥ 75 years). In the sensitivity analysis, the double-robust adjusted ORs in patients of ≥ 65 , ≥ 70 , and ≥ 75 years old was respectively 0.35, 0.14 and, thus, the above adjusted ORs was conservative and not overestimating.

Discussion

This study found that the PPSV23 prevented non-IPD in older patients (age ≥ 65 years) with chronic respiratory diseases, and could be more effective for the elderly (patients aged ≥ 70 years). To the best of our knowledge, this is the first real-world study that assesses the effectiveness of the PPSV23 in older patients with chronic respiratory disease in a single center.

In previous studies, the effectiveness of the vaccine against pneumococcal pneumonia was controversial. In the results of a meta-analysis of 18 randomized trials [4], the PPSV23 reduced the risk of IPDs such as bacteremia, meningitis, and bacteremic pneumonia (OR [95 % CI]: 0.26 [0.15–0.46]) and non-IPD (0.46 [0.25–0.84]). However, some studies reported that the PPSV23 did not reduce non-IPD [5, 6, 9]. The EVAN-65 study in community-dwelling patients [10] showed that the hazard ratios (HR) for the risk of pneumococcal pneumonia in vaccinated patients compared with non-vaccinated patients were not different (HR [95 % CI]: 0.61 [0.35–1.06]). Similarly, another study in elderly patients with chronic respiratory diseases showed no difference (0.76 [0.30–1.90]) [11]. These conflicting results can be due to the difficulties of accurately diagnosing pneumococcal pneumonia and the use of non-validated diagnostic tests [12]. In this study, we included non-invasive cases according to specific diagnostic criteria of pneumonia, urine pneumococcal antigen, and sputum culture, and we are convinced that these results are close to correct.

One previous case-control study suggested that 85–90 % of adults aged 55 and younger achieved the prevention of invasive pneumococcal infections, but this effectiveness was reduced with increasing age, and no protection was shown in the population aged ≥ 80 years [13–15]. These studies suggest that poorer effectiveness might be due to immunosenescence, which refers to the decline of the immune system associated with aging [16]. However, this study found that the OR was much decreased in older people, which could imply that older people can acquire antibodies with the PPSV23 vaccination, and we proposed that older people be re-vaccinated because of an anticipated decline in the effectiveness of the vaccine over time.

Almost all patients with chronic respiratory diseases in this study had risk factors for pneumonia [17]. Previously, most studies on the PPSV23 targeted nursing home residences or healthy adults, and

controversial results have been reported on non-invasive pneumonia [7]. Our findings suggest the importance of vaccinating chronic respiratory patients in clinical practice.

There were several limitations. First, this study was a retrospective single-center study, and a complete confounding adjustment was not done. Second, we did not assess the severity of the underlying diseases. The study population was biased, consisting mainly of moderate to severe disease cases. Third, we did not regularly identify the serotype of each pneumococcal pneumonia.

In summary, the PPSV23 was useful in preventing non-IPD among the elderly with chronic respiratory diseases and in patients ≥ 85 years.

Declarations

Author contributions

Study concept and design: TM, EN, TS; acquisition of data: TM, TS, TA, KT, ST, YT, HW, YE, TS, MS, AY, SM, KA; data analysis: TM, EN, YS; interpretation of data: TM, EN, YS, TS; first draft of the manuscript: TM; All authors reviewed and approved the final manuscript for submission.

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Availability of data and materials

The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This study conforms to the Ethical Principles for Medical Research Involving Human Subjects issued by the Ministry of Health, Labour and Welfare and the Ministry of Education, Culture, Sports, Science, and Technology in Japan. Following these guidelines, the Shizuoka General Hospital Research Ethical Committee determined that individual patient informed consent was not required because this study was an analysis study of existing information and patients were given the right to refuse participation by disclosure. After obtaining the approval of this committee (SGHIRB#2017062) and publishing the disclosure document on Shizuoka General Hospital's website, the information of each individual was anonymized, and the analysis was conducted.

Consent for publication

Not applicable.

Competing Interest

The authors have no conflicts of interest to disclose.

Acknowledgments

Not applicable.

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Figures

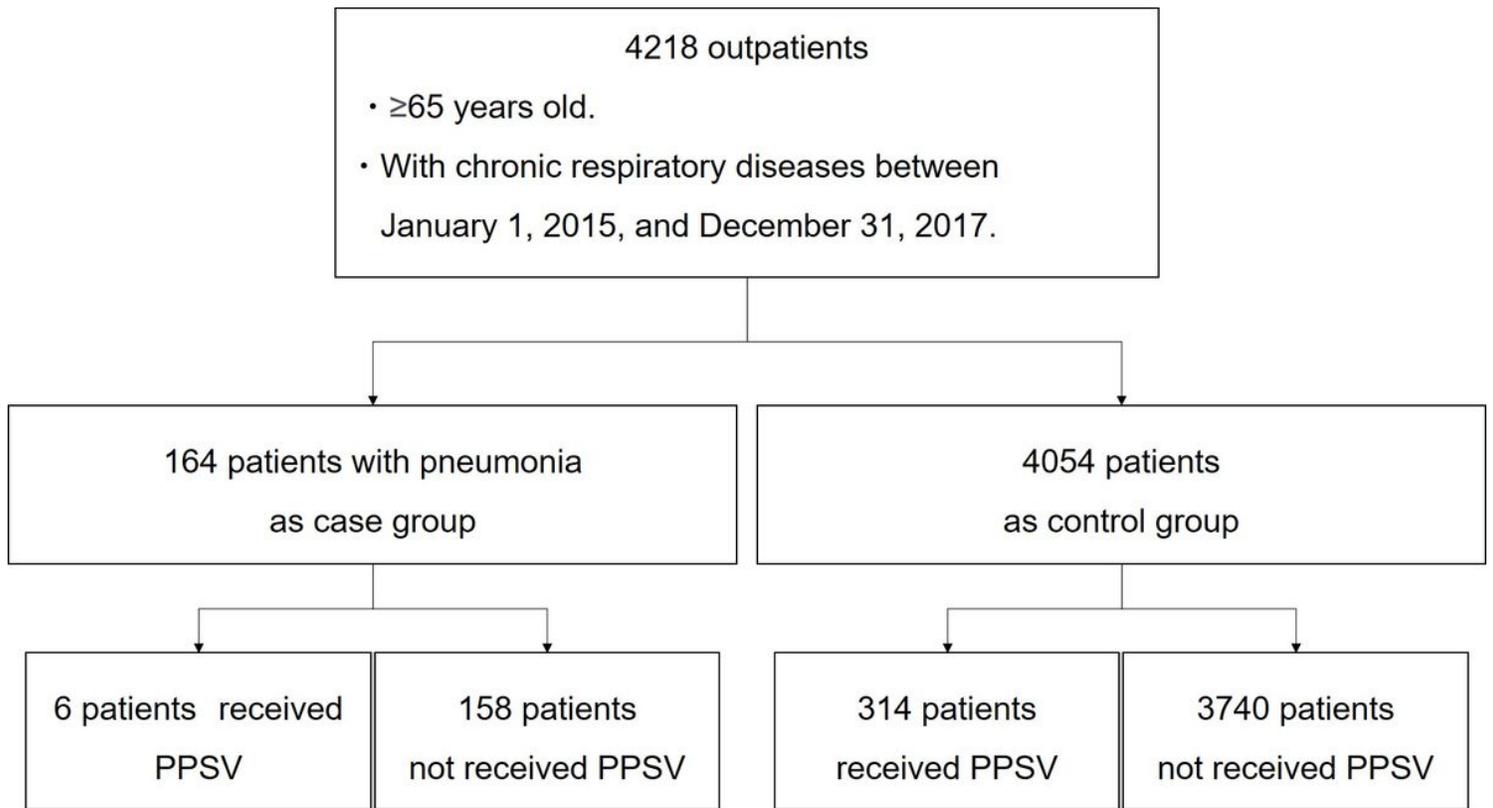


Figure 1

Patient flow. PPSV23: 23-valent pneumococcal polysaccharide vaccine

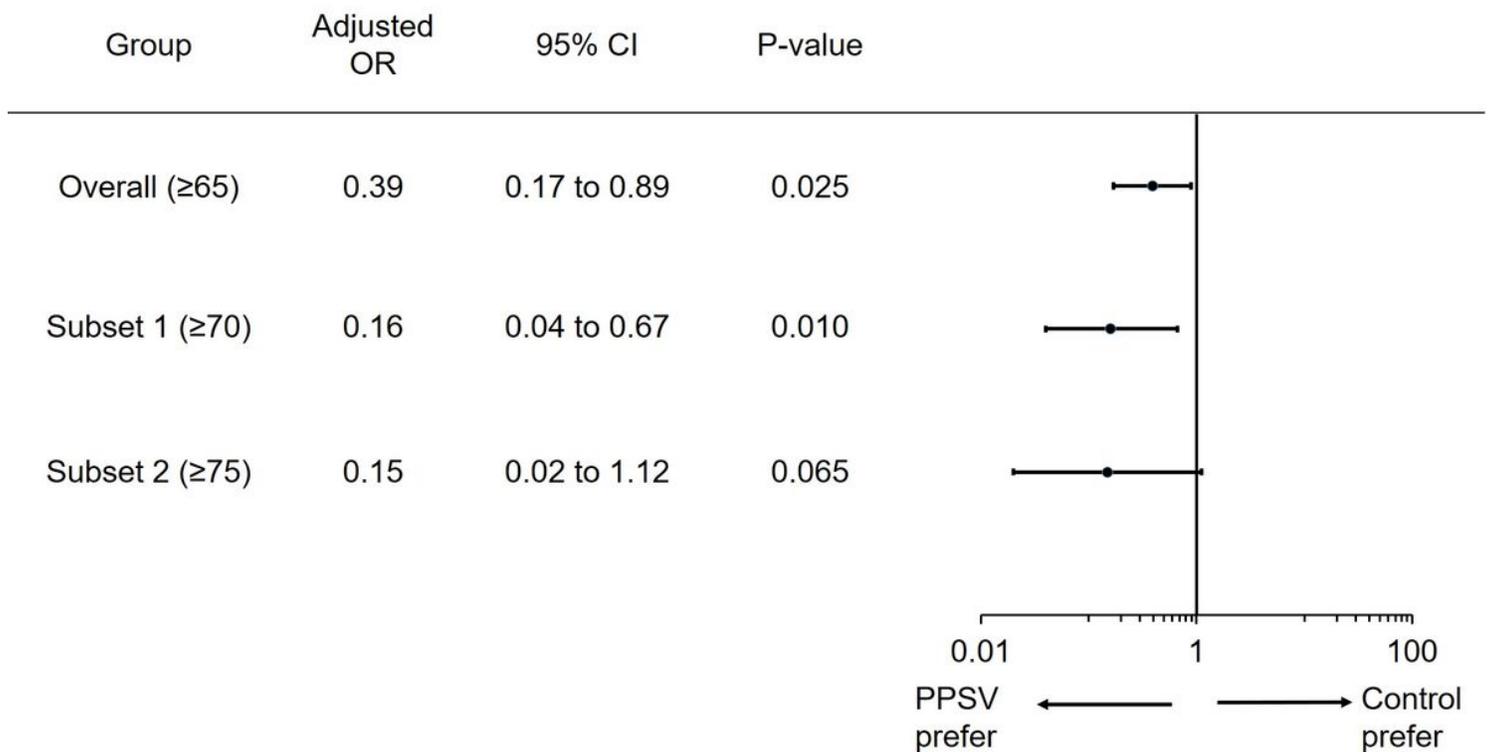


Figure 2

Effectiveness of vaccines in pneumococcal pneumonia in age-related subsets. OR: odds ratio, CI: confidence interval, PPSV23: 23-valent pneumococcal polysaccharide vaccine. The lower adjusted ORs in subsets of older patients were estimated, suggesting that the PPSV23 can be more effective for older patients. The adjusted OR was adjusted using the quantile category of propensity scores.