THE NEW ARMENIAN MEDICAL JOURNAL
Vol.13 (2019), No 1, p. 85-90

POLYSACCHARIDES PNEUMONIA VACCINATION (PPV-23) AND SERUM PNEUMONIA-SPECIFIC IGG LEVELS IN THE ELDERLY

Merlyna Savitri[1], Jusri Ichwani[2], Ari Baskoro[3], Gatot Soegiarto[3*]

[1] Department of Internal Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya, Indonesia

[2] Division of Geriatric Medicine, Department of Internal Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya, Indonesia

[3] Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya, Indonesia

Received 15.12.2018; accepted for printing 10.01.2019

Abstract

Background: Immune responses in elderly will decline with increasing age, which eventually leads to increased susceptibility to infections. Respiratory tract infections such as pneumonia are the leading cause of death and decreased quality of life in the elderly. Pneumococcal vaccination is highly recommended by the WHO for the elderly, but previous report showed a poor response. Currently there is still limited data about the effect of pneumococcal polysaccharides (PPV-23) vaccination to the serum pneumococcal-specific IgG levels in the elderly.

Objevtives: To determine the effect of the PPV-23 vaccination on the serum pneumococcal-specific IgG levels in elderly hajj pilgrims in Indonesia.

Methods: This is a pre-posttest study involving healthy older hajj pilgrims recruited from 5 community health centers in Gresik, East Java, Indonesia during the 2012 hajj season. All eligible subjects gave their written consent. PPV-23 vaccination were given before depature. Serum pneumococcal-specific IgG levels were measured using ELISA method before and 4 weeks after the vaccination.

Rsults: We recruited 21 elderly hajj pilgrims (age > 60 years), consisted of 12 females and 9 males. The median serum pneumococcal-specific IgG levels before vaccination was 2029 mU/mL (range: 441-2918 mU/mL), which significantly increased to 3251 mU/mL (range: 2251-8110 mU/mL) after vaccination. The median increase in serum pneumococcal-specific IgG levels was 1222 mU/mL which was statistically significant (p = 0,000; Wilcoxon test).

Cnclusion: Vaccination with pneumococcal polysaccharides (PPV-23) significantly induce an increase in the serum pneumococcal-specific IgG levels in Indonesian elderly hajj pilgrims.

Keywords. *elderly; pneumococcal vaccinations (PPV-23); serum pneumococcal-specific IgG*

Introduction

According to the World Health Organization (WHO) elderly population is defined as people with > 60 years old. The number of elderly population is growing in many parts of the world. Current population of Indonesia is 225,000,000, and 7.6% of which or 17,100,000 persons are the elderly. By 2025 it is estimated that Indonesia's elderly population will be around 13.1% of the population (1). The immune response in the elderly will decline with age which known as immunosenescence. Clinical implications of immunosenescence include increased susceptibility to infection and poor response to vaccination (2). Elderly are particularly susceptible to respiratory infections, especially pneumonia, which is the leading cause of death and the most significant cause of the decline in quality of life (3-6). The elderly individuals who perform hajj pilgrimage have a high risk of developing pneumonia infection due to high transmission factors and extreme weather. Pneumonia is the most commonly acquired infection in elderly hajj (7). Another study in 2003 reported that 19.7% of the subjects got pneumonia, and 1 patient died due to pneumonia (8).

In the elderly, the decreased immune response lead

Address for Correspondence:
Gatot Soegiarto MD., Ph.D.
Division of Allergy and Clinical Immunology, Department of Internal Medicine, Faculty of Medicine Universitas Airlangga, Dr. Soetomo General Hospital, Surabaya 60286, Indonesia.
Tel.: (+6231) 5501617; (+6281)23547784
Email: gatotsby@yahoo.com
ORCID ID: http://orcid.org/0000-0002-9197-3873

to more severe infections. That is why the vaccination to prevent infection, especially pneumonia, becomes very important (4). Unfortunately, the effectiveness of pneumonia vaccination in the elderly is still debatable. Meta-analyses failing to provide robust evidence on vaccine efficacy against invasive pneumococcal disease (IPD) or pneumonia. The signs and symptoms of pneumonia in the elderly are often atypical which often lead to a delay in diagnosis. This situation have a very significant impact, such as longer treatment periods, higher maintenance costs, and frequent complications that often arise (3-6, 9).

The immune response to pneumococcal vaccination can be measured by various parameters such as the increase in serum pneumococcal-specific IgG levels or the protective effects of vaccination on the incidence of pneumonia infection. The immune response to the pneumococcal polysaccharide vaccine (PPV-23) in various age groups, including the elderly, had been studied previously (10). The effectiveness of vaccination can be evaluated by conducting clinical trials, which is not easy to do (11). The evaluation of serum pneumococcal-specific antibody levels after vaccination can be measured with ELISA (3, 10-12). The results of previous studies are conflicting and discordant. Our study aimed to determine the effect of the PPV-23 vaccination on serum pneumococcal-specific IgG levels in elderly individuals who will perform the hajj pilgrimage and evaluate the incidence of pneumonia infection during the hajj pilgrimage.

METHODS

This was a pre-post test clinical study in Indonesian elderly hajj pilgrims conducted at 5 community health centers in Gresik and Kebomas sub-district, Gresik regency, East Java Indonesia during the 2012 hajj season between September-November 2012. Using simple random sampling method, we recruited the study subjects. Eligible subjects were individuals aged >60 years old who agree to have pneumococcal polysaccharide (PPV-23) vaccination and willing to give their written consent. Subjects with one or more of the following conditions, i.e. have a history of allergy to components of the vaccines, diabetes mellitus, chronic obstructive pulmonary disease, heart failure, history of alcohol consumption, active smokers, received long-term corticosteroid drugs, immunodeficiency condition (such as HIV infection or malignancy), and patients with malnutrition, were excluded from the study. Serum pneumococcal-specific IgG levels were measured using ELISA method (ZenTech S.A., Liege Science Park 4031, Angleur, Belgium) before and 4 weeks after PPV-23 vaccination (Pneumovax 23, Merck Sharp & Dohme Corp., Whitehouse Station, NJ, USA). We use the World Health Organization (WHO) recommended guideline for quantification of IgG antibodies specific to pneumococcal PS (PnPS) for laboratory ELISA examintation as described elsewhere (12). All of the adverse effects of PPV-23 vaccination were collected and recorded.

Data with normal distribution were analyzed using paired t-test, while data with abnormal distribution were analyzed using Wilcoxon test. The statistical test was done using SPSS 12 program (SPSS, Inc., Chicago, IL.). The results were considered significant when p value <0.05.

RESULTS

There were 21 subjects from 5 community health centers in Gresik regency that fulfilled the inclusion and exclusion criteria and can be followed-up until the end of this study (4 weeks). The majority of them was female (57.1%). The median of the age of the study subjects was 63 years (range: 60 – 76 years). In general, there were no significant electrocardiogram (ECG) abnormality

TABLE 1.

Characteristics of study subjects

Variables	Median (min-max)	% (n = 21)
Age (year)	63 (60-76)	
Body mass index (kg/m^2)	24.0 (18.5-30.5)	
Hemoglobin (gr/dL)	13.5 (10.0-15.6)	
Leukocytes count (µL)	7500 (4000-10.900)	
Platelets count (µL)	262,000 (150,000-377,000)	
Fasting blood sugar (gr/dL)	126 (94-164)	
Electrocardiogram		
Normal		90.5%
Old miocardial infarction		4.8%
Right bundle branch block		4.8%
Chest-X ray		
Normal		100%

and the chest-X ray were normal. Other characteristics of the subjects were summarized in Table 1.

Pre and post-vaccination serum pneumococcal-specific IgG levels

Vaccination with PPV-23 significantly increase the level of serum pneumococcal-specific IgG in elderly hajj pilgrims. The increase in antibody level were observed in 18 subjects (85.7%). The data had an abnormal distribution. Median pre-vaccination serum pneumococcal-specific IgG level was 2029 mU/mL. After vaccination, the median was increased to 3251 mU/mL (Table 2). This change was statistically significant (p=0.000, Wilcoxon test).

Adverse effects of PPV-23 vaccination

After PPV-23 vaccination there were some minor adverse effects reported by study subjects. Three subjects reported the presence of fever (14.2%), and one subject suffered from pain (4.76%) or itchy (4.76%) at the sites of injection. The majority of the subjects (85.7%) had no complaints. At the end of the study period, only one subject reported that he suffered from acute upper respiratory tract infection during the hajj pilgrimage (Table 3).

Prevention of respiratory infection and pneumonia after PPV-23 vaccination

After PPV-23 vaccination there was only one subject (4.76%) reported to have acute upper respiratory tract infection and one subject (4.76%) suffered from pneumonia and hospitalized at Saudi Arabia during the hajj pilgrimage. Most of the other subjects (90.48%) did not have any complaints (Table 3).

Table 2.

Pre- and post-vaccination serum pneumococcal-specific IgG

	median (mU/mL)	min-max
Pre-vaccination	2029	441- 2918
Post-vaccination	3251	2251 - 8110

Table 3.

Adverse effects and incidence of illness after PPV-23 vaccination

Parameters	n	%
Adverse effects		
Reported adverse effect	3	14.2
Fever	1	4.76
Pain at injection site	1	4.76
Itching at injection site	1	4.76
Reported no adverse effect	18	85.7
Incidence of illness		
Acute upper respiratory tract infections	1	4.76
Pneumonia (hospitalized)	1	4.76
Reported no major illness	19	90.48

Discussion

Our study evaluated the serum pneumococcal-specific IgG before and after pneumococcal polysaccharide (PPV-23) vaccination in elderly Indonesian hajj pilgrim. The results showed that PPV-23 vaccination significantly increase the antibody levels and quite protective. Only one PPV-23 vaccinated subject suffered from pneumonia and hospitalized during the study period.

Although only involving a relatively small samples, the gender composition in our samples (57.1% females compared to 42.9% males) was consistent with the gender composition of the elderly population in Indonesia. According to elderly demographic data in Indonesia in 2013, there were 15,454,360 elderly population which consisted of 7,963,594 elderly females (51.5%) and 7,490,766 elderly males (48.4%). This data showed that our samples were really represent the elderly Indonesian population.

The median age of our study subjects was 63 years (range: 60-76 years). This data also showed concordance with the data of the 2012 hajj pilgrims at Gresik district health office, where 305 elderly pilgrims (14.98%) participated from a total of 2035 hajj pilgrim from the area in that year. In the 2003 hajj pilgrimage season, as many as 808 pilgrims had to be hoptilazised in Mina and Arafah of Saudi Arabia due to severe illness, in which 47 persons of them (5.8%) were Indonesians. The majority of the hospitalized hajj pilgrims (309 persons or 38.2%) were elderly people (age >60 years). Pneumonia was detected and diagnosed in 159 persons (19.7%), resulting in 1 death from pneumonia (8).

Regarding other factors that may influence the health and the immune status of the study subjects, the median body mass index (BMI) in our study was 24.00 kg/m2 (ranged: 18.5-30.5 kg/m2) which is fall within normal category, and indicates an adequate nutritional status. Our study subject also had normal leukocyte count, showing that they were healthy old individuals. With these conditions we can expect a good response to vaccination although they belong to the elderly persons.

The immune response to PPV-23 vaccines in vari-

ous age groups, including the elderly had been studied previously (11). The antibody response to PPV had been investigated as a marker of vaccine protection. Pneumococcal serotype-specific antibodies that provide protection in vaccinated people are the antibodies to capsular polysaccharides (CP) (13, 14). For the evaluation of PPV-23 vaccination in this study, we measured the pneumococcal-specific IgG in the serum using ELISA method as has been done in some previous studies (3, 10-12). There were significant increase in median serum pneumococcal-specific IgG levels from 2029 mU/mL (range: 441-2918 mU/mL) before vaccination up to 3251 mU/mL (2251-8110 mU/mL) after vaccination (p=0.000).

Until now there were still no consensus on the level of serum pneumococcal-specific IgG needed to provide protective effect against S. pneumoniae (16, 17). Serum pneumococcal-specific IgG levels between 0.1-3.5 μg/mL proved to have a protective effect against S. pneumoniae infection in vivo (16). Our study showed that after PPV-23 vaccination in the elderly, the median serum pneumococcal-specific IgG levels was 3251 mU/mL (range: 2251-8110 mU/mL), and can be considered as quite effective because only one subject (4.76%) had pneumonia infection during study period. This findings was also concordant with the results of another study comparing specific IgG concentration in 46 healthy elderly and 12 young individuals after PPV-23 vaccination. Mean pre-vaccination specific IgG concentrations in the elderly was 2.5 μg/mL which increased to 5.1 μg/mL after vaccination (10). Despite serum pneumococcal IgG level increase in elderly individuals at 3 weeks after PPV-23 vaccination, the IgG levels of elderly persons still lower than younger individuals. Research on 53 elderly individuals without control showed an increase in mean serum pneumococcal IgG level at 4 weeks after vaccination from 3.77 μg/mL to 8.20 μg/mL (12). These suggest that antibody response to PPV-23 vaccine in elderly population was still adequate.

In our study, the PPV-23 vaccine was generally safe and cause only minor adverse effects such as fever, pain and itching. The majority (85.7%) of our study subjects had no complaints after vaccination. This is consistent with the study on 9336 elderly individuals in Northern Ireland, in which 4581 subjects received influenza vaccination alone and 4775 subjects received influenza and pneumococcal vaccinations. Around 72% (95% CI: 71-80%) of subjects that received influenza and pneumococcal vaccines suffered from mild local adverse events, 19% (95% CI: 15-23%) of them had moderate adverse events, and only 5% (95% CI: 4-8%) had severe adverse events. Systemic side effects such as fever were observed in 4.32% of the subjects receiving influenza and pneumococcal vaccinations (18).

Our study was also aligned with another study of 139 elderly individuals who received influenza and pneumococcal vaccination. Twenty nine individuals reported adverse effects, 12.9% of them experienced local side effects (pain, erythema, and hematoma) and 12.9% of them suffered from systemic side effects (fever, headache, arthralgia, myalgia) (19).

In our study, only one subject (4.76%) had pneumonia infection and hospitalized during hajj pilgrimage, showing a good protective effect against pneumococcus. Our finding was consistent with the study of Consonni et al., which reported that only 2.15% of their elderly subjects admitted to hospital due to pneumonia (19). This was also consistent with the meta-analysis done on 13 clinical trials involving 65,000 patients, 7 clinical trials on elderly subjects showed that pneumonia vaccination using pneumococcal polysaccharide vaccine (PPV-23) can be expected to reduce the risk of systemic infection due to pneumococcal types included in the vaccine by 83% and systemic infection due to all pneumococci by 73% (20). We also come to the same conclusion that there was no evidence that the vaccine was less efficacious for the elderly, as previously thought.

In the elderly, there are several known risk factors for community-acquired pneumonia including the decline of the immune function. Many aspects of the body defense are declining in the elderly: reduced capability to produce antibodies, reduced mucocilliary clearance, and changed respiratory mechanic. Besides the presence of comorbids that predispose to bronchial aspiration (such as stroke), all of those factors may contibute to the high incidence of bronchial aspiration in the elderly. Bacterial colonization of the upper respiratory tract by gram-positive and gram-negative bacteria are often found in elderly individuals and are associated with the severity of systemic disease. Comorbid diseases such as chronic obstructive pulmonary disease, im-

munosuppressant drug use, smoking, heart failure, diabetes mellitus, malignancy, and history of previous hospitalization due to CAP are the independent risk factors for the occurrence of pneumonia. this disease (22, 23). In our study, all of those risk factors were screened and excluded, which might contribute to the low incidence of pneumonia in our elderly subjects. Nevertheless, the increase in serum pneumococcal-specific IgG levels after PPV-23 vaccination in our study was a prove that this vaccine was not less efficacious for the elderly.

Conclusion

Vaccination with pneumococcal polysaccharides (PPV-23) significantly increase serum pneumococcal-specific IgG levels in elderly hajj pilgrims and prevent them against pneumococcus infection.

REFERENCES

1. *Fatmah.* Respon Imunitas Tubuh yang Rendah pada Tubuh Manusia Usia Lanjut. Makara. 2006;10:47-53.
2. *Wardwell L, Chapman-Novakofski K, Herrel S, Woods J.* Nutrient intake and immune function of elderly subjects. Journal of the American Dietetic Association. 2008;108(12):2005-12.
3. *Simonsen V, Brandao AP, Brandileone MC, Yara TI, Di Fabio JL, Lopes MH, et al.* Immunogenicity of a 23-valent pneumococcal polysaccharide vaccine in Brazilian elderly. Brazilian Journal of Medical and Biological Research = Revista Brasileira de Pesquisas Medicas e Biologicas. 2005;38(2):251-60.
4. *Soejono CH.* Upaya pencegahan penyakit pada warga usia lanjut: Perhatian khusus pada influenza dan pneumonia. Supartondo SS, Sari NK, Mansjoer A, Harimurti K, Laksmi PW editor. Jakarta: Pusat Informasi dan Penerbitan Bagian Ilmu Penyakit Dalam FKUI; 2005. 116-24 p.
5. *Clarke SC.* Control of pneumococcal disease in the United Kingdom--the start of a new era. Journal of Medical Microbiology. 2006;55(Pt 8):975-80.
6. Perhimpunan Gerontologi Medik Indonesia. Konsensus Nasional Imunisasi untuk Usia Lanjut. *Soejono CH BA, Djauzi S, Makmun LH, Setiati S, Wahyudi ER, Ginawati L,* editor. Jakarta: Divisi Geriatri Penyakit Dalam RSCM FKUI; 2009. 1-13 p.
7. *Al-Ghamdi SM, Akbar HO, Qari YA, Fathaldin OA, Al-Rashed RS.* Pattern of admission to hospitals during muslim pilgrimage (Hajj). Saudi Medical Journal. 2003;24(10):1073-6.
8. *Madani TA, Ghabrah TM, Al-Hedaithy MA, Alhazmi MA, Alazraqi TA, Albarrak AM, et al.* Causes of hospitalization of pilgrims in the Hajj season of the Islamic year 1423 (2003). Annals of Saudi Medicine. 2006;26(5):346-51.
9. *McCullers JA.* Insight into the interaction between influenza virus and pneumococcus. Clinical microbiology reviews. 2006;19:571-82.
10. *Romero-Steiner S MD, Cetron M, Pais L, Groover J, Fiore A,.* Reduction in functional antibody activity against Streptococcus pneumoniae in vaccinated elderly individuals highly correlates with decreased IgG antibody avidity. Clinical Infectious Diseases. 1999;29(5):281-8.
11. *Lee H, Nahm MH, Kim KH.* The effect of age on the response to the pneumococcal polysaccharide vaccine. BMC Infect Dis. 2010;10:60.
12. *Rubins JB, Alter M, Loch J, Janoff EN.* Determination of antibody responses of elderly adults to all 23 capsular polysaccharides after pneumococcal vaccination. Infection and Immunity. 1999;67(11):5979-84.
13. *Artz AS, Ershler WB, Longo DL.* Pneumococcal vaccination and revaccination of older adults. Clinical Microbiology Reviews. 2003;16(2):308-18.
14. *Pletz MW, Maus U, Krug N, Welte T, Lode H.* Pneumococcal vaccines: mechanism of action, impact on epidemiology and adaption of the species. International Journal of Antimicrobial Agents. 2008;32(3):199-206.
15. *Mathews CE, Brown EL, Martinez PJ, Bagaria U, Nahm MH, Burton RL, et al.* Impaired function of antibodies to pneumococcal surface protein A but not to capsular polysaccharide in Mexican American adults with type 2 diabetes mellitus. Clinical and Vaccine Immunology. 2012;19(9):1360-9.

16. *Marchese RD, Jain NT, Antonello J, Mallette L, Butterfield-Gerson KL, Raab J, et al.* Enzyme-linked immunosorbent assay for measuring antibodies to pneumococcal polysaccharides for the PNEUMOVAX 23 vaccine: assay operating characteristics and correlation to the WHO international assay. Clinical and Vaccine Immunology. 2006;13(8):905-12.

17. SCHENKEIN JG, NAHM MH, DRANSFIELD MT. Pneumococcal vaccination for patients with COPD: current practice and future directions. Chest. 2008;133(3):767-74.

18. HONKANEN PO, KEISTINEN T, KIVELA SL. Reactions following administration of influenza vaccine alone or with pneumococcal vaccine to the elderly. Archives of Internal Medicine. 1996;156(2):205-8.

19. *Consonni S SC, Segato E, Perucchini E, Bergamaschini L, Vergani C,*. Tolerability and efficacy of anti-influenza vaccination alone and associated with antipneumococcal vaccination in an elderly ambulatory population and adherence to the vaccination campaign. Journal of Preventive Medicine and Hygiene. 2004;45:45-50.

20. *Hutchinson BG OA, Shannon HS, Llyod S, Altmayer CA, Thomas K,*. Clinical effectiveness of pneumococcal vaccine: meta-analysis. Canadian Family Physician. 1999;45:2831-93.

21. *Christenson B, Hedlund J, Lundbergh P, Ortqvist A.* Additive preventive effect of influenza and pneumococcal vaccines in elderly persons. The European Respiratory Journal. 2004;23(3):363-8.

22. *Jackson ML, Neuzil KM, Thompson WW, Shay DK, Yu O, Hanson CA, et al.* The burden of community-acquired pneumonia in seniors: results of a population-based study. Clinical Infectious Diseases. 2004;39(11):1642-50.

23. *Janssens JP, Krause KH.* Pneumonia in the very old. The Lancet Infectious diseases. 2004;4(2):112-24.