Prevention of Pneumonia through Vaccination

Introduction

Pneumococcal infections are the major cause of morbidity and mortality. Prevention of community-acquired pneumonia (CAP) in high-risk populations is the urgent need of the hour, especially in India, where tuberculosis has acquired endemic proportions in some regions. Thus, there is considerable interest in the prevention of CAP through appropriate vaccination.

Pneumococcal Disease

About 1.6 million cases of fatal pneumococcal disease occur worldwide annually based on 2002 WHO estimate, mostly in infants and the elderly. Also, immunocompromised individuals are at increased risk of pneumococcal disease irrespective of age. Pneumococcal disease can be noninvasive or invasive. Invasive pneumococcal disease (IPD) is characterized by the presence of S. pneumoniae in blood, cerebrospinal fluid or another normally sterile body site.

The incidence of invasive disease is higher in those with functional or anatomic asplenia and in immunocompromised people. The latter group includes those with inherited immune deficiency as well as those with acquired immune deficiency due to conditions such as cancer, immunosuppressive chemotherapy or HIV infection.

The annual incidence of IPD ranges from 8 to 34 cases/100,000 population, with the highest rates occurring in infants and children aged <2 years and in the elderly in industrialized countries. The incidence is much higher in the developing countries. Therefore, prevention becomes an important aspect of management of pneumococcal disease.

Vaccines have a significant effect on the incidence of pneumococcal infections. Control through vaccinations has gained importance because despite of appropriate antimicrobial therapy and intensive care, mortality in severe pneumococcal infections remains high. Also, there has been an increasing pneumococcal resistance to essential antimicrobial drugs.

Pneumococcal Pneumonia Vaccines

Currently available pneumococcal vaccines are of two types:

1. Polysaccharide vaccines
2. Conjugate vaccines

Polysaccharide Vaccines

Pneumococcal polysaccharides are T-cell-independent antigens and thus are poorly immunogenic in those aged <2 years and fail to induce immune memory. Therefore, revaccination can be considered for polysaccharide vaccines as demonstrated in some studies.

WHO-commissioned meta-analysis and a review of RCTs of PPV23 demonstrate a protective effect against IPD and all-cause pneumonia among generally healthy young adults and, to a lesser extent, protection against IPD in the general population of elderly people. However, high-quality RCTs are unable to highlight its protective effects in those adults at the highest risk of pneumococcal infection.

Polysaccharide vaccines are found to be safe in older children and non-pregnant adults. Polysaccharide vaccines are indicated for the protection of healthy elderly people, patients with chronic organ failure, particular immunodeficiencies, prevention of subsequent pneumococcal pneumonia and children at high risk of disease (splenectomized, sickle cell disease).

Pneumococcal Conjugate Vaccine

Protein conjugated antigens induce T-cell-dependent response against polysaccharide antigens in infants and elderly people. Since the introduction of Pneumococcal conjugate vaccine 7 (PCV), the incidence of IPD, pneumococcal meningitis, pneumonia, and bacteremias has declined. The declines in adults were dramatic and may be attributed to herd immunity.

According to WHO, PCVs should be preferred for inclusion in national immunization programs. Pneumococcal conjugate vaccine with broader serotype coverage like PCV13 should be considered. According to a study, PCV7 covers only 44% of serotypes responsible for pneumococcal disease whereas PCV13 covers 78% of serotypes responsible for pneumococcal disease. The major advantage of PCV13 is its extended coverage including 19A serotype, which is increasingly becoming resistant to antibiotics.

Recommendations

The pneumococcal conjugate vaccine is recommended to be administered at 6, 10 and 14 weeks followed by the booster dose at 15 months.

A 13-valent pneumococcal conjugate vaccine (PCV13) has been recently approved for use in older adults in India. The vaccine is indicated for active immunization, for the prevention of pneumonia and invasive disease, caused by S. pneumoniae serotypes 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F and 23F, in adults of 50 years and older.

The clinical trials of PCV13 have been reviewed by Sanford. According to the review, in immuno-competent, pneumococcal vaccine-naive adults aged 60–64 years and previously vaccinated adults aged ≥70 years, the immune response provoked by PCV13 was noninferior to that of the PPV23 vaccine. The PCV13 provoked a stronger immune response than PPV23 for the majority of serotypes common to the vaccines, and for serotype 6A. Immune responses to PCV13 in adults aged 50-59 years were noninferior to those in adults aged 60-64 years.

Immune responses to PCV13 and PPV23 administered in different sequences indicate that if both vaccines are to be used, PCV13 should be administered first. Based on immunogenicity findings from a randomized trial, PCV13 can be administered concomitantly or after vaccination with trivalent influenza vaccine. Across trials, adverse events with PCV13 were generally of mild-to-moderate severity. Concomitant administration of PCV13 with trivalent influenza vaccine was associated with a higher incidence of systemic adverse events than sequential administration of the vaccines.

Role of Vaccination for CAP in Elderly Patients

The burden of CAP in elderly is high and needs to be addressed on an emergency basis. A Finnish trial reports that the incidence of pneumococcal CAP was 9 per 1000 person-years (4 per 1000 person-years in low-risk individual and 19 per 1000 person-years in high-risk individuals) in this population.
Community-acquired pneumonia in adults is most commonly caused by *Streptococcus pneumoniae*. The high-priority issue for health policy makers worldwide is the effective prevention of pneumococcal CAP and IPD through vaccination. This study also indicated that randomized trials were inadequately designed to establish the effects of vaccination on IPD, while about 30-45% effectiveness has been indicated in a meta-analysis. Non-randomized studies on 23-valent polysaccharide pneumococcal vaccine (PPV23 or 23vPS) have shown a significant effect on reduction of CAP in elderly population.

**Revaccination in Elderly**

There is an increase in the case fatality rate of IPD from 20% (aged >65 years) to 40% (aged >85 years) as age progresses. Pneumococcal polysaccharide vaccines have shown about 50-70% effectiveness in preventing IPD in elderly individuals among different serotypes. However, there is a controversy with the effectiveness of the pneumococcal polysaccharide vaccine (PPV) in older population.

A retrospective case-control study indicates that protection against IPD by vaccine serotypes after five years is about 85% in individuals aged 55 years, while it is about 58% in individuals aged 65-74 years and about 13% in 85-year-old individuals.

### Vaccination in Patients with Obstructive Airways Disease (Chronic Obstructive Pulmonary Disease and Asthma)

Chronic obstructive pulmonary disease (COPD) patients are at high risk of pneumococcal infections, whereas asthma patients are not at high risk. The magnitude of the increased risk in COPD is decreased by pneumococcal vaccination.

Vaccination in COPD patients is supported in a study by Niewoehner et al. whereas vaccination in asthma patients is not favored.

This study also put forth some useful guidelines for vaccination in COPD. These guidelines are summarized as follows:
- Pneumococcal vaccination in COPD is recommended in all patients with COPD except those who are hypersensitive to any component of vaccine.
- Pneumococcal vaccination is recommended once or twice in lifetime for patients above 65 years of age.
- One-time revaccination is recommended for patients aged 65 years and more, or 5 years since the first vaccination, or age at the time of first vaccination being less than 65 years. There was no benefit of pneumococcal vaccination in reducing COPD exacerbations as indicated from meta-analysis data.

A significant reduction in hospitalizations for pneumonia and in risk of death in individuals with chronic lung disease was seen with pneumococcal vaccination in a large cohort study, whereas another study did not demonstrate reduction in hospitalizations with the use of pneumococcal vaccination.

### Guidelines for Influenza Vaccinations in COPD

- Influenza vaccination is recommended for all patients with COPD. It is not advised for individuals with hypersensitivity to any component of vaccine, especially eggs. Influenza vaccine is given annually. The best time would be before influenza season or at any time throughout season.
- Substantial reduction in influenza-related respiratory illnesses with influenza vaccinations in COPD patients is established in data from a meta-analysis. Another cohort study has shown that influenza vaccination reduces hospitalizations for pneumonia. In the same study, it was seen that influenza and risk of death during influenza season in individuals with chronic lung disease were associated.

### Vaccination for Pneumococcal Infections in Diabetes Patients

Diabetes mellitus is an independent risk factor for developing respiratory tract infections and is a well-known risk factor for pneumococcal infection as it predisposes individuals to nasopharyngeal colonization with the pneumococcus (which is associated with invasive infection).

Diabetes patients respond properly to pneumococcal vaccination, and vaccination is a cost-effective preventive strategy. In comparison to unvaccinated individuals, patients vaccinated with pneumococcal polysaccharide vaccine were found to have a reduction in risk of infections by 84%. A recent Indian study has shown that pneumococcal polysaccharide vaccine 23 was associated with a significant protection against recurrent lower respiratory infections, exacerbations of COPD and hospitalizations.

### Smoking Cessation and CAP Risk Reduction

Consumption of tobacco is an important risk factor for CAP and the development of COPD in adults. The odds ratio of CAP in a population-based case control study was 2.0 for ever smokers, 1.88 for current smokers and 2.14 for ex-smokers. An increase in the duration of the habit, the average number of cigarettes smoked daily and cumulative cigarette consumption further increased the risk of CAP.

There is a 50% reduction in the odds ratio of the risk of CAP 5 years after the cessation of smoking. Smoking cessation activities are important for the prevention of CAP.

### Global Recommendations

World Health Organization recommends the use of polysaccharide vaccine for adults aged above 65 years, patients with chronic organ failure and immunodeficient patients recovering from pneumococcal infection. According to the European recommendations, single dose of PPV is advised for individuals at the age of 65 years. Polysaccharide vaccine is recommended for adults aged above 65 years and also one or two doses for the age group of 2-65 years in the United States.

### Indian Recommendations

Use of 23 valent PPV is recommended for adults over 50 years of age by the Geriatric Society of India. Pneumococcal vaccination is recommended for diabetes patients at an increased risk (older patients, nephropathy, renal insufficiency and malignancy) according to the Diabetic Association of India.

### Recommendations

- Pneumococcal vaccination is recommended for adults over 50 years of age. It is recommended for diabetes patients at increased risk (older patients, nephropathy, renal insufficiency and malignancy).
Revaccination of all adults aged 65 years and older (five years since the first vaccination and age at the time of first vaccination being less than 65 years is recommended.

References
6. Prevenar 13 prescribing information. Wyeth limited, India. CDS Version 9.0; April 2012