

## Editorial

# Vaccines in Chronic Respiratory Diseases

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Asthma, COPD, occupational lung diseases, pulmonary hypertension and sleep apnea syndrome are listed as the commonly encountered chronic respiratory diseases (CRD) worldwide as per WHO reports.<sup>1</sup> The prevalence of these diseases is increasing everywhere particularly among children and elderly people. The most common chronic respiratory diseases are asthma and COPD. These preventable CRD'S cause premature deaths and disabilities and may account for more than 4 million deaths a year worldwide.<sup>1</sup> COPD is currently the fourth leading cause of mortality worldwide and is predicted to be the third leading cause of global mortality by 2020.<sup>2</sup>

Statistics reveal that there is a 60 to 65 % reduction in the death rates due to coronary heart disease and stroke in USA in the last 30 years due to effective strategy for prevention and control of coronary artery diseases, whereas there is about 50 % increase in death rates due to COPD. People with obstructive airway disease may be affected by a wide range of respiratory viruses and bacteria. Streptococcus pneumonia and influenza viruses are the major etiological agents identified for frequent exacerbations and worsening disease status. Pneumococcal and influenza infection cause substantial morbidity and mortality particularly among people having co morbid illnesses.<sup>3</sup>

People with obstructive airway diseases are at a higher risk of invasive pneumococcal disease (IPD) while those with COPD have the same risk for influenza infection as others. However, they are more likely to have complications following influenza infections. Influenza and pneumococcal infections contribute to acute exacerbation of asthma and COPD leading to increased risk of hospitalizations and mortality. Although streptococcus pneumonia and influenza are not the most common respiratory pathogens for most of the exacerbations, they are important as they are potentially preventable by vaccination.<sup>4</sup>

## Influenza Vaccination

As influenza A (H1N1), A (H3N2) and influenza B viruses are all currently circulating worldwide, currently available formulations of influenza vaccine are trivalent.<sup>2</sup> Two types of trivalent influenza vaccines are available for the prevention of influenza.

Trivalent Live Attenuated, cold adapted Influenza Vaccine (LAIV)

Trivalent Inactivated influenza Vaccine (TIV)

LAIV is administered intranasally and may be used to vaccinate healthy non pregnant persons. Although LAIV has been studied in persons with COPD, safety has not been clearly established.

Quadrivalent inactivated vaccine (QIV) contains 4 strains of influenza, that is two sub types of A strains (H1N1, H3N2) and two types of B strains (Victoria, Yamagata). There is also quadrivalent live attenuated influenza vaccine (Q LAIV) which is available as a nasal spray.<sup>4</sup>

Influenza infection is estimated to account for 10 to 30% of exacerbations of Asthma and COPD. Both GINA and GOLD guidelines and many countries recommend annual influenza vaccinations for persons with Asthma and COPD regardless of age and disease severity.<sup>5</sup>

Vaccination with TIV has been found to be safe in asthmatics, specifically with regards to the concern of development of frequent acute asthma exacerbations. Because of lack of safety data, LAIV is not currently recommended for use in people with asthma. One of the randomized trials found an increasing clinically relevant wheezing among those younger than 24 months within 24 hours after receiving LAIV, regardless of whether they had asthma or not.<sup>6</sup>

It has been found that vaccination against influenza improves health related quality of life among children with asthma. Influenza vaccine has to be administered annually before the influenza season because the strains of the virus in circulation change from year to year.<sup>3</sup>

Influenza vaccination is associated with 45% reduction in mortality in patients with COPD. Influenza vaccination reduces specific mortality due to pneumonia in COPD and in addition reduces all cause mortality due to stroke, diabetes and renal diseases. Despite the recommendation for annual vaccinations against influenza, more than half of the patients with COPD in developed countries do not receive this vaccine.<sup>8</sup>

In a study of 1,77,120 patients with COPD (mean age 65 years ) with a mean follow up of 6 to 8 years between 1988 and 2006, it had been observed that influenza, but not pneumococcal vaccination was associated with reduced risk of all cause mortality in COPD.<sup>9</sup>

## **Pneumococcal vaccination**

*Streptococcus pneumoniae* is a major cause of morbidity and mortality worldwide in causing lower respiratory tract infections. Despite appropriate antibiotic therapy and intensive care treatment, mortality rates due pneumococcal infection remains high especially in older adults and high risk individuals such as patients with CRD. COPD is one of the major risk factors for community acquired pneumonia. Smoking is reported to be an important risk factor for invasive pneumococcal disease.<sup>10</sup>

More over patients with COPD who develop pneumonia could have more severe pneumonia with higher frequency of ICU admissions. In addition there is higher case fatality rate than non COPD patients. Approximately 15 % of acute exacerbations in chronic bronchitis are triggered by bacterial infections and pneumococci is responsible for almost one third of acute bacterial exacerbations.<sup>10</sup>

**There are three types of anti pneumococcal vaccinations.**

**Capsular polysaccharide pneumococcal vaccines (PPV / PPSV).**

**Protein polysaccharide conjugate pneumococcal vaccine (PCV).**

**Protein based pneumococcal vaccine (PBPV).**

The pneumococcal polysaccharide vaccine used today for older children and adults is 23 valent and is effective against 23 types of pneumococci. The 23 valent PPS (PPV 23 / PPSV 23)

vaccine protects against 85 to 90 % of the types of pneumococci that cause invasive infection in these age groups. Polysaccharide vaccines are not effective in children younger than 2 to 3 years of age for whom Conjugate vaccines were developed.<sup>10</sup>

PCV7 targeted the 7 most common types of pneumococci which accounted for 80 to 85 % of invasive diseases in infants and toddlers. Although the vaccine is generally given to children aged 2 years, it is wise to give conjugate vaccine to infants as young as 6 months.<sup>20</sup> The new pneumococcal conjugate vaccine PCV 13 contained 6 more additional strains and was developed to replace PCV7.

All people aged 65 years or older, adult smokers and adults with CRD should ideally receive PPV 23 vaccine.<sup>10</sup> People 2 years or older who are at increased risk of pneumococcal disease due to conditions like chronic heart, kidney or liver diseases should also receive PPV 23. Immunocompromised state like diabetes, alcoholism, HIV infection, Sickle cell disease, defects of splenic function are other conditions in which PPV vaccination is recommended.<sup>10</sup>

Infants and children 2 to 59 months of age who have not previously received PCV 7 or PCV 13 should receive PCV 13. Among patients with CRD, pending other more effective anti pneumococcal vaccines, PPV23 (together with influenza vaccine) is currently the only preventive option that has demonstrated considerable beneficial effects though the effect is not 100%. Revaccination (5 to 10 years after primary dose) is recommended for those persons who receive PPV23 below 65 years of age. PPV 23 provides only incomplete protection as it does not elicit long lasting immunity and there is no anamnestic effect at revaccination. Therefore more effective vaccination strategies are needed. The experimental protein based pneumococcal vaccine candidates offer the potential advantage of serotype independent protection.

Clinical practice guidelines recommend vaccination against pneumococcal infection as an important component of management of COPD (GOLD 2013). Pneumococcal vaccine has been shown to reduce the risk of pneumococcal infection among patients with COPD aged 65 and above with reduction in the incidence of community acquired pneumonia in patients with COPD younger than the age of 60 who have severe airflow limitations (FEV1 less than 40% predicted).

Subset analyses of randomized controlled trials showed that combination of pneumococcal and influenza vaccine when compared to influenza vaccine alone reduces infectious acute exacerbations among people with COPD. Evidence of reduction in asthma exacerbations with pneumococcal vaccination is less clear. However a retrospective study found an association between pneumococcal vaccine and reduction in the number and duration of hospitalization for asthma among elderly.<sup>3</sup>

Recipients of both influenza and pneumococcal vaccinations were associated with 63 % reduction in the risk of hospitalization for pneumonia and 81% reduction in the risk of death when compared with those unvaccinated.<sup>2</sup> Vaccination among people with CRD is less than 50 % in developed countries. Barriers to vaccination are patient barriers and physician barriers. To improve the uptake of vaccinations among people with chronic respiratory diseases in our country, an effective strategy for prevention and control of these has to be developed and implemented.

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