Prevention and treatment of Pneumococcal disease

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Abstract

Pneumococcal disease has a worldwide mortality rate of around 1,6 million people annually. Infection with S. pneumoniae results in pneumococcal diseases such as pneumonia, meningitis, bacteraemia and acute otitis media. The burden of pneumococcal diseases and increasing resistance to antibiotics is a reminder that prevention of pneumococcal disease through vaccination is becoming increasingly important, particularly in overcrowded communities with a high incidence of malnutrition.

Prof Nurs Today 2017;21(3):13-17

Introduction

Pneumococcal disease results in around 600 000 deaths in children younger than 5 years of age, with the majority of deaths occurring in Africa.[1] Childhood vaccination with pneumococcal conjugate vaccines has led to a declining mortality in adults 18–64 years of age. However, the outcome of invasive pneumococcal disease in the elderly and those with other associated risks has remained essentially unchanged for several decades.[2] This article discusses pneumococcal disease, its prevention, and its treatment.

What is pneumococcal disease?

Pneumococcal disease is caused by infection with *Streptococcus pneumoniae (S. pneumoniae,* also known as pneumococcus), a gram positive encapsulated lancet-shaped coccus, that usually occurs in pairs (diplococci). Based on differences in the composition of the capsule, there are more than 90 different serotypes of pneumococci. *S. pneumoniae* is spread from the nasopharyngeal area of the carrier via respiratory droplets after sneezing or coughing.[3]

Pneumococcal disease may cause non-invasive illness if it spreads from the nasopharynx to the upper- and lower-respiratory tract. Non-bacteraemic pneumonia, sinusitis and acute otitis media are all non-invasive pneumococcal diseases.[4]

If *S. pneumoniae* invades the blood stream, or otherwise sterile sites such as the cerebrospinal fluid, diseases such as bacteraemia (sepsis), meningitis and bacteraemic pneumonia result.[4] *S. pneumoniae* is estimated to cause around 35% of all community-acquired pneumonias in Europe.[2,5] Other infections that are rarely caused by pneumococcal infection include osteomyelitis, pericarditis, arthritis and soft tissue infections.[6]

Who is at risk?

The following factors may increase the risk of contracting pneumococcal disease:

- Age: Children under the age of 2 years and the elderly (older than 65) are at increased risk of contracting pneumococcal disease. Pneumonia in these age groups is mainly caused by *S. pneumoniae*.
- Underlying medical conditions: Patients with diabetes, chronic pulmonary diseases (including asthma), cardiovascular disease and cerebrospinal fluid leaks as well as immunocompromised patients such as HIV positive (human immunodeficiency virus) patients, patients with sickle cell disease, children with cochlear implants, patients with immunosuppressive disorders such as Hodgkin's disease, lymphoma, multiple myeloma, malignant neoplasms or solid organ transplant patients; those with chronic renal failure, and nephrotic syndrome are all predisposed to pneumococcal disease.[5,7]
- Ethnic group: Certain racial groups such as the Aboriginals, Asians, Blacks, Hispanics, Native Alaskans, White Mountain

Apaches and Navajo Native Americans have a higher risk of contracting pneumococcal disease than Caucasians.[5]

- Social/ environmental: The winter season as well as excessive exposure to tobacco smoke (including passive exposure), indoor fuel exposure and malnutrition are also contributing risk factors, predisposing patients to pneumococcal disease.[4] Overcrowded living conditions and child care centres also increase the risk of contracting pneumococcal disease. Children exposed to more than two non-related children for longer than 4 hours per week are considered to be at higher risk.[4]

How can pneumococcal disease be prevented?

In South Africa, the high number of HIV positive patients, overcrowded living conditions, high rates of malnutrition and the ever-increasing resistance to antibiotics makes it more difficult to treat pneumococcal infections. Therefore, it is imperative to prevent people from contracting pneumococcal disease.[3,5]

Education on avoiding tobacco smoke and indoor fuel exposure (indoor fires, etc.) and maintaining adequate nutritional status, especially during times of illness, is necessary to reduce the incidence of pneumococcal disease. Exclusive breastfeeding for 6 months is a low-cost way to ensure sufficient nutrition in infants. Zinc plays a key role in immune function and supplementation with zinc in children under 5 years of age may reduce the incidence of pneumonia.[3] In addition, vaccination against pneumococcal disease is recommended to reduce the incidence of pneumococcal disease.

Vaccination with pneumococcal vaccines

According to the World Health Organization (WHO), more than 70% of all invasive pneumococcal diseases are caused by approximately 20 serotypes of *S. pneumoniae*.[1,5] Two types of vaccines are currently available for vaccination in South Africa. These are the conjugated pneumococcal vaccines and the 23-valent polysaccharide vaccine for use in children older than 2 and in adults who are at high risk of pneumococcal disease.[8,9,10]

Pneumococcal conjugated vaccine (PCV)

Since bacterial polysaccharides, such as the pneumococcal capsule, are T-independent antigens, and because children respond poorly to T-independent antigens, the polysaccharides are conjugated to other proteins to increase effectiveness of the PCV in children. The conjugation changes the antipolysaccharide response from T-independent to a T-dependent response, resulting in a substantial primary response and a strong booster response in children.[11]

HIV positive children are 20 to 40 times more likely to acquire pneumococcal disease and despite the reduced immune response, prevention acquired by PCV in HIV positive children is around ten times greater than the prevention acquired by PCV in normal healthy children.[5]

The Center for Disease Control and Prevention (CDC) recommend administration of PCV-13 to all children from the age of 6 weeks through 59 months of age.[6,11] In addition, PCV-13 is also recommended for children 6 years and older who are at increased risk of contracting pneumococcal disease.[11] (See above). Side effects after vaccination usually occur within 48 hours after vaccination and tend to be limited to the site of injection. These include pain, erythema, tenderness, oedema, inflammation and skin discolouration. Urticaria, dermatitis and pruritis have also been reported. Fever, irritability, restless sleep, drowsiness, vomiting, diarrhoea and decreased appetite are some of the systemic side effects reported after vaccination.[12]

South Africa introduced the PCV-7 vaccine as part of the National Expanded Programme for immunisation (EPI) with effect April 2009. This was replaced by the 13-valent pneumococcal conjugate vaccine (PCV-13) in April 2011.[1] A 10-valent pneumococcal conjugate vaccine (PCV-10) is also registered for use in infants and children in South Africa.[13]

PCV vaccines are contra-indicated in patients with a history of severe allergic reaction to any of the ingredients in the vaccine, including diphtheria toxoid. Although duration of immunity after vaccination with PCV is unknown, immunologic memory does occur.[11]

23-valent pneumococcal polysaccharide vaccine (PPV23)

The 23-valent pneumococcal vaccine is registered for use in children from the age of 2 years and older.[9,10] The vaccine protects against 23 strains of *S. pneumoniae* that cause 85–90% of invasive pneumococcal diseases in adults. The vaccine also provides immunity against some of the most common antibiotic-resistant strains.[5]

Several factors complicate optimal vaccine schedules. Effectiveness of the vaccine decreases with age and antibody titres tend to decline to approximate pre-vaccination levels within 4 to 7 years after vaccination. Additional uncertainty as to the possible hypo-responsiveness to revaccination and inconsistent data on efficacy of the vaccine further complicates recommendations on an optimal vaccination schedule for PPV23.

The current recommendation for primary vaccination with PPV23 is a single dose of vaccine administered either subcutaneously (SC) or intramuscularly (IM) into the deltoid muscle. IM administration is preferred as the incidence of adverse events was found to be less than with SC administration. The vaccine is recommended for high-risk patients (see above) and adults over the age of 65. In high-risk patients, a single revaccination is recommended 5 years after the initial vaccination.[5]

In South Africa, the use of antiretroviral treatment and chemoprophylaxis with cotrimoxazole in the HIV positive population may lower the risk of *Pneumocystis jiroveci* pneumonia (PCP) and patients are not routinely vaccinated with PPV23. These measures together with routine vaccination of children with PCV provide indirect protection to adults and other unvaccinated members of the community.[4,5]

According to the CDC, a dose of PPV23 vaccine in addition to the PCV-13 administered at least 8 weeks after the last dose of PCV13 is also recommended in high-risk children over the age of 2 years with underlying medical conditions. This includes patients with cochlear implants.[11] PCV-13 and PPV23 should not be administered at the same visit.[7] Recommendations for PCV-13 and PPV23 depend on age and risk factors. When both are recommended, it is preferable to administer PCV-13 first, followed by PPV23 where possible. Longer intervals may be recommended based on which vaccine was given first as well as the patient's age and immune status.[14]

Treatment of pneumococcal disease

Pneumococcal pneumonia

Although several organisms may cause pneumonia, *S. pneumoniae* remains the most common, causing 58% of pneumonia cases in the elderly. Early treatment of pneumococcal disease reduces hospitalisation rates, morbidity and mortality of the disease. Education of caregivers and healthcare workers to identify and treat children with pneumococcal disease appropriately is crucial. Coughs and colds may be treated at home, but fast breathing, chest in-drawing and wheezing should be assessed at a clinic or by the doctor. Caregivers should be counselled on the importance of compliance with treatment and must be told to bring the child back if there is no response to treatment or if the condition worsens.[15]

In the elderly, less than 60% of patients may display common symptoms of pneumonia (i.e. cough, fever, and dyspnoea). The following atypical symptoms should be considered possible signs of pneumonia in the elderly[15]:

- Confusion, delirium and deterioration of function, e.g. in performing usual daily activities
- Falls
- New or worsening incontinence
- Worsening of comorbidities such as cardiac failure

Younger patients without co-morbid disease may be treated at home, usually with high doses of amoxicillin. Older patients and patients with chronic underlying disease, including HIV may be treated at home with amoxicillin-clavulanic acid combinations, oral cephalosporins or fluoroquinolones.[15]

Hospitalisation should be considered for patients presenting with one or more of the following:

- Children younger than 2 months or adults older than 65 years.
- Underlying chronic disease such as HIV, chronic cardio-respiratory disease, diabetes, renal or liver disease.
- Cyanosis, confusion or decreased level of consciousness, low blood pressure, tachypnoea or any other symptoms indicating severe pneumonia.
- Complications of infections.[15]

Children older than 2 months should be taken to the clinic or hospital immediately if the child with suspected pneumococcal disease is:[3]

- unable to drink or breastfeed
- lethargic or unconscious
- having convulsions
- vomiting.

Treatment of pneumonia is based on antibiotics and the choice depends on the causative organism. Treatment of choice in children older than 2 months is amoxicillin. In patients with underlying co-morbidities or resistance, moxifloxacin or cephalosporins (ceftriaxone, cefotaxime) may be indicated. In severely ill patients, clavulanic acid, aminoglycosides and macrolide antibacterials may be added. Due to high resistance of *S. pneumoniae* to macrolides, they are not recommended as monotherapy in South Africa.[15]

Pneumococcal meningitis

Whilst pneumococcal pneumonia is the most common pneumococcal disease, pneumococcal meningitis is the most serious and deadly.[4] Inflammation of the lining surrounding the brain and spinal cord leads to symptoms that may include fever, headache, stiff neck, seizures, lethargy, confusion, nausea and vomiting and an aversion to bright lights.[3]

For *S. pneumoniae*, South African standard treatment guidelines for adults recommend treating with benzylpenicillin. If resistance is present, ceftriaxone should be administered for at least 10 days instead of benzylpenicillin. In case of penicillin allergy, chloramphenicol may be used, and if *S. pneumonia* is resistant to chloramphenicol, vancomycin and rifampicin should be used. Supportive treatment in the form of appropriate analgesia (with paracetamol and/ ibuprofen and/ or morphine), as well as oxygen therapy and when necessary treatment for the control of convulsions may be necessary.[16]

Pneumococcal acute otitis media

Pneumococcus used to be the major cause of acute otitis media.[3,17] Since the introduction of pneumococcal vaccination in 2009, *Haemophylis influenzae* has replaced

S. pneumoniae as the most frequently isolated pathogen causing middle ear infection.[17]

In less severe cases, due to the prevalence of antibiotic resistance, observation for 48 hours with symptomatic treatment may be sufficient treatment, except where acute otitis media (AOM) is associated with a bulging tympanum and a temperature > 38˚C. Systemic ibuprofen or paracetamol may be used to relieve pain and, if necessary, local anaesthetics such as benzocaine or lignocaine ear drops may also be applied for quick relief. First-line antibiotic treatment for acute otitis media is amoxicillin. In patients with penicillin allergy, any of the macrolides may be recommended. Children under the age of 2 years should be treated with antimicrobials for 7 days, and children older than 2 years for 5 days.[17,18]

Antihistamines and decongestants have not been proven to improve healing or prevent complications and are not recommended for the treatment of AOM. Antihistamines may also prolong the duration of middle ear effusion.[18]

In conclusion

The high incidence of pneumococcal disease together with the increase in development of antibiotic resistance, underlines the necessity and urgency of prevention of pneumococcal disease. Vaccination with PCV to protect vaccinated children as well as unvaccinated contacts by reducing the spread was introduced by the Department of Health in April 2009 and has substantially reduced the incidence of pneumococcal disease in South Africa.[19]

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