An Update of Hospital–Acquired Pneumonia (HAP): a Review

Nada Khairi Younus
Pharmacy Department/Al-noor university collage/Mosul/Iraq
nada.khairi@alnoor.edu.iq

Summary

Progress has been made in the prevention and treatment of community-acquired bacterial meningitis during the past three decades but the burden of the disease remains high globally. Conjugate vaccines against the three most common causative pathogens (Streptococcus pneumoniae, Neisseria meningitidis, and Haemophilus influenzae) have reduced the incidence of disease, but with the replacement by non-vaccine pneumococcal serotypes and the emergence of bacterial strains with reduced susceptibility to antimicrobial treatment, meningitis continues to pose a major health challenge worldwide. In patients presenting with bacterial meningitis, typical clinical characteristics (such as the classic triad of neck stiffness, fever, and an altered mental status) might be absent and cerebrospinal fluid examination for biochemistry, microscopy, culture, and PCR to identify bacterial DNA are essential for the diagnosis. Multiplex PCR point-of-care panels in cerebrospinal fluid show promise in accelerating the diagnosis, but diagnostic accuracy studies to justify routine implementation are scarce and randomized, controlled studies are absent. Early administration of antimicrobial treatment (within 1 hour of presentation) improves outcomes and needs to be adjusted according to local emergence of drug resistance. Adjunctive dexamethasone treatment has proven efficacy beyond the neonatal age but only in patients from high-income countries. Further progress can be expected from implementing preventive measures, especially the development of new vaccines, implementation of hospital protocols aimed at early treatment, and new treatments targeting checkpoints of the inflammatory cascade.

1. Introduction

Streptococcus pneumonia is pathogenic bacteria, One of Streptococcus which is a genus of gram-positive cocci or spherical bacteria that belongs to the family Streptococcaceae, within the order Lactobacillales, in the phylum Firmicutes. Cell division in streptococci occurs along a single axis, so as they grow, they tend to form pairs or chains that may appear bent or twisted. These bacteria are lancet-shaped, facultative anaerobic organisms, observed in pairs, some pneumococci are encapsulated, and their surfaces composed of complex polysaccharides. Streptococcus pneumoniae surrounded by a polysaccharide capsule that allows the micro-organism to avoid phagocytosis, representing a major virulence factor; moreover, capsular variability permits different subtypes to avoid immune detection by antibodies previously generated by infection or administration of vaccine. The most common origin of infection was the respiratory tract, followed by the intra-abdominal region [1]. In November 08, 2020, a new information were published about (HAP), Hospital-acquired pneumonia (HAP) is often more severe and life-threatening than community-acquired pneumonia (CAP). There is a review focused on considerable morbidity and mortality that caused by nosocomial pneumonia or hospital-acquired pneumonia (HAP) [2]. It is the second most common nosocomial infection and the leading cause of death from hospital-acquired infections and the most frequently involved pathogens were Enterobacteriaceae, Haemophilus influenzae, Streptococcus pneumoniae and Staphylococcus aureus ('core pathogens'). Studies that have appeared since the American Thoracic Society (ATS) statement issued in 1996, demonstrate several new risk factors for Hospital-acquired pneumonia (HAP) with multiresistant pathogens. In patients with risk factors, empirical therapy should consist of antibacterials with a broader spectrum. The most important risk factors for resistant microorganisms are late onset of Hospital-acquired pneumonia (HAP) 5 days or more after admission, recent use of antibacterial therapy, and mechanical ventilation, and empiric antibiotic treatments should be selected based on the local data and the distribution of pneumonia among people [3, 4]. Another review paper shed light on different cases of patients with unusual pneumococcal infections, like pancreatic and liver abscesses, aortitis, gingival lesions, phlegmonous gastritis, inguinal adenitis, testicular and tubo-ovarian abscesses, and necrotizing fasciitis. The common risk factors for invasive pneumococcal infections are alcoholism, HIV infection Splenectomy, connective tissue disease, steroid use, diabetes mellitus, and intravenous drug use [5].

The objective of this review was to summarize the publications and update the HAP infections by *S. pneumonia* in hospitals among patients.

2. Risk Factors and Pathogenes

This bacterium has the ability to adhere to mucosal linings as an important virulence factor [6]. *Streptococcus pneumoniae* is a major cause of pneumonia, meningitis, sinusitis, and acute otitis media, as well as a frequent cause of bacteremia. Many studies have delineated epidemiological, clinical, and prognostic characteristics of community-acquired pneumococcal bacteremia [1].This agent cause meningitis and septicemia can kill in hours with symptoms like fever, vomiting, headache and feeling unwell. Limb pain, pale skin, and cold hands and feet often appear earlier than the rash, neck stiffness, dislike of bright lights and confusion. Schuchat et al. [7] Patients

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with depression of their immune function were in high-risk if they infect their respiratory tract, bloodstream and central nervous system by *Streptococcus pneumonia* as a cause of nosocomial infectious agent [6]. Patients with pneumococcal infections acquired from hospitals were associated with high mortality specially the AIDS patients. Pneumonia is an inflammation of the lungs involving the alveolar ducts and sacs and lead to death in difficult cases [8]. The pathogens are varied; Mycoplasma pneumonia is the primary cause of pneumonia among children and adults. The second type of agent is Streptococcus pneumonia. The other type of bacteria are *Staphylococcus aureus* that present in hospital acquired pneumonia11 %(HAP) as well as community acquired-pneumonia 2.5 %(CAP). *Haemophilus influenza*, *Klebsiella pneumonia*, *Escherichia coli* and *pseudomonas aeroginosa* all are emerged as pathogens that cause pneumonia with the other types like viruses and fungi in intensive care units [9]. In 2005, the researchers reported the main risk factors for the specific pathogens of (HAP), for example: the risk factor for *Streptococcus aureus* that lead to coma, head trauma, recent influenza.

3. Methodology

We conducted a review of published Streptococcus pneumoniae which represent as a secondary cause of HAP.

4. Etiology

Is Streptococcus pneumoniae a nosocomially acquired pathogen? The answer was documented in 1998, Streptococcus pneumoniae is most prominently a major cause of community-acquired infections of the respiratory tract, and penicillin- resistant pneumococcal strains appeared three decades ago and spread worldwide. The centers for Disease Control in 2008 issued that a major cause of morbidity and mortality globally causing more deaths by pneumococcus bacteria and the highest risk are the smallest children and the elderly. Many studies have hypothesized that toddlers are the infectious reservoir for the pneumococcus, and transmitting it to other people [10]. Indeed, in elderly patients up to 20% of hospital-acquired pneumonia is due to S. pneumoniae. Nosocomial pneumonia was judged directly responsible for lethal outcome in 19% of patients and a contributing factor to death in another 13% [11].This bacteria surely leads to death by infect people and cause bacteremia (Pneumococcal bacteremia). Between 1975 and 1980, Scientists from University of Pittsburgh School of Medicine, Pennsylvania reported that the mortality rate was 43 percent by Pneumococcal bacteremia among adults most of them were men from surgical hospital [12]. A similar study mentioned that the mortality rate related to hospital-acquired pneumococcal bacteremia was 39% during 1988 to 2000. All patients had underlying diseases that predisposed them to pneumococcal infection. The important point that we should understand is the distribution of etiologic agents that cause nosocomial pneumonia differs between hospitals because of different patient populations and diagnostic methods used [13]. The incidence of pneumonia in males was higher than in females because of the difference in social status between the sexes. Both viruses and bacteria are transmitted by contact with infected respiratory secretion (person-to person contact) [14]. February was the peak month and from October until February the rate of pneumonia admission is high rate and the most common etiology of pneumonia were S. pneumonia and M. pneumonia. The most important reason is low temperature in winter [8].

Diagnosis; microbiology and molecular testing

In 1800 Streptococcus pneumonia was first identified, recognized and diagnosed from many patients with lobar pneumonia. In the medical laboratories all samples from lung secretions should be treated for identification of Streptococcus pneumonia started from culture to observe both its morphological appearance and four main important phenotypic characteristics, including α-hemolysis of blood agar, catalase negativity, optochin susceptibility, and bile solubility. The finding of optochin-resistant pneumococci has decreased the utility of this characteristic as a distinguishing feature, but overall these phenotypic markers are quite reliable [15]. Many microbial studies showed different difficulties in recovering S. pneumoniae in culture media, including the tendency of S. pneumoniae to autolyse when reaching the stationary phase of growth, antibiotic treatment prior to specimen collection, and in the case of lower respiratory tract infection (LRTI), difficulty with adequate specimen collection and the low prevalence of detectable bacteremia in community-acquired pneumonia (CAP). But culture techniques have a number of advantages, including the ability to implement them worldwide with low cost and high specificity, as well as the ability to provide both antibiotic susceptibility and serotype data.

In conclusion, nowadays there are newer test have been developed that use antigen-based or molecular detection method for identification of S.pneumoniae [15]. Also the direct detection of S.pneumoniae from the pleural fluid, bronchoalveolar lavage (BAL) by using a technique known as group C polysaccharide antigen test showed the good results and it is a better alternative method than urinary antigen test that designed for isolation and detection of Streptococcus .pneumoniae from children [16-19]. For diagnosing of Streptococcus pneumonia samples will be isolating the organism from blood, body fluids to detect capsular polysaccharide antigen. By the most familiar method PCR (polymerase chain reaction) S.pneumoniae has been detected by finding specific pneumococcal genes. This PCR, based on and depend on the amplification of species-specific genes that are unique to the pneumococcus. Many genes like pneumolysin gene (ply) have been detected successfully from pneumococcal disease patients [20]. But, after many researches and medical studies, they found that ply gene can be detected in non-pneumoncoccal Viridans-group streptococci [21, 22]. These findings lead to the question of whether the poor performance of pneumolysin-based PCR for the detection of pneumococcal disease is related to limitations of molecular testing itself, or to the poor specificity of the assay. Later, autolysin gene (lytA), the pneumococcal surface adhesion gene (psaA), and the

spn9802 gene fragment had been detected successfully [23-25]. Note that S. pneumoniae detection is depend on or conjunction with clinical information or symptoms like fever, cough, and respiratory distress. The microbiology of HAP is reviewed, with an emphasis on multidrug resistant pathogenic strains (MDR) for other types of bacteria in addition to S.pneumonaie. These types of bacteria are Pseudomonas aeruginosa, Acinetobacter species, and methicillin-resistant Staphylococcus aureus MRSA that make problems in respiratory tract of human [1].

In future, for rapid detection of Pneumococcal infection, we recommended using another molecular typing method, such as whole-genome sequencing (WGS), PFGE, or MLST. The best one is (WGS) [26]. We all know that the patient's case history and chest X-ray, respiratory symptoms and clinical features are very helpful to confirm the diagnosis of pneumonia [14].

Treatment and risk factors for antibiotic resistance

Pneumonia that acquired from hospitals develops at least 48 hours after hospital admission. Researchers classify pneumonia in to Community-acquired pneumonia (CAP), Hospital-acquired pneumonia (HAP), (excluding ventilator-associated) Ventilator-associated (VAP), and Aspiration pneumonia (AP) which occurs when large volumes of upper airway or gastric secretions enter into the lungs. These categorizations allow treatment to be selected empirically.

Regarding antibiotics susceptibility such as penicillin, erythromycin, clindamycin and cefotaxime were used for treating HAP patients with bacteremia. Many resist strains of S.pneumoniae were detected and treated. Also there are many difficult cases with patients such as multilobar pneumonia, infection of ascitic fluid, neoplasia, and leukopenia lead to death although they had treated by antibiotics, because of pneumonia resist strains [1]. There are two patterns which are used in treatment of (HAP); first one local sensitivity patterns and the second is patient risk factors for antibiotic-resistant pathogens i.e. the chosen of antibiotics that are used for the treatment of (HAP) are dependent on and based on these two patterns. In 2016 they use a narrow spectrum of empiric antibiotics for hospital-acquired pneumonia without increasing risk for antibiotic-resist bacteria. While in the 2007 the Infectious Diseases Society of America (IDSA) and the American Thoracic Society (ATS) used very broad criteria for defining the population at risk of infection with antibiotic-resistant pathogens, which resulted in the majority of patients with HAP requiring broad-spectrum antibiotic therapy for Methicillin- resistant Staphylococcus aurous (MRSA) and resistant Pseudomonas aeruginosa. The types of antibiotics that are empirically recommended are Piperacillin/tazobactam, Cefepime, Levofloxacin, Imipenem, and Meropenem [27].

General Prophylaxis

In one paper I found many important recommendations for the management of hospital-acquired pneumonia (HAP), ventilator-associated pneumonia (VAP) and healthcare-associated pneumonia (HCAP). These recommendation points were prepared by American Thoracic Society (ATS) in 1996 which supported by Infectious Diseases Society of America (IDSA), focuses on the epidemiology and pathogenesis of bacterial pneumonia in adults, and emphasizes modifiable risk factors for infection. In general the major goals of these recommendations are for management of HAP, VAP, and HCAP emphasize early, appropriate antibiotics in adequate doses, while avoiding excessive antibiotics, based on microbiologic cultures and molecular technique and the clinical response of the patient, and shortening the duration of therapy to the minimum effective period. Depending on many studies scientists recognized that the excessive antibiotic use inappropriate way in hospitals without physician treatment lead to increase the frequency of antibiotic- resistant pathogenic strains. Because pneumonia is the second most common and important nosocomial infection in hospitals and is associated with real morbidity and mortality among infants, young children, and old persons; patients suffering from severe underlying disease, immunosuppression, depressed sensorium, and/or cardiopulmonary disease; and patients who have had thoraco-abdominal surgery; patients receiving mechanically assisted ventilation which are at highest risk for acquiring infection, "Guideline for Prevention of Nosocomial Pneumonia" have been updated and replaces CDC's then published to reduce the incidence of hospital Acquired pneumonia among patients and is designed and intended for use by personnel who are responsible for surveillance and control of infections in acute-care hospitals. Many important points in this manual focused on decreasing aspiration by the patient; preventing cross-contamination or colonization via hands of personnel; appropriate disinfection or sterilization of respiratory-therapy devices; use of available vaccines to protect against particular infections; and education of hospital staff and patients. One of the most important and accurate strategy to reduce the HAP infection is vaccination. Patients at high risk for complications of pneumococcal infections should be vaccinating with pneumococcal polysaccharide vaccine (PPV). Who included in this program are patients have chronic cardiovascular or pulmonary disease, diabetes mellitus, alcoholism, cirrhosis, or cerebrospinal fluid leaks; and children and adults who are immunosuppressed or who have functional or anatomic asplenia or HIV infection. Nowadays, the Advisory Committee on Immunization Practices (ACIP) has revised its recommendations to include the use of 13-valent pneumococcal conjugate vaccine (PCV13) in adults and infants [28].

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