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A Systematic Review On The Management Of Community Acquired Pneumonia

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Abstract

Pneumonia is a widespread and continuing health burden caused by lung inflammation. In India, there were 3.3 million cases of pneumonia in 2021 with a projected decrease to 2.2 million by 2030. India accounts for 23% of the global pneumonia burden and 36% of the WHO regional burden for patients under five years. Reported fatalities range from 14-30% in CAP patients and 47% in SCAP patients. Treatment options include beta lactam mono therapy, beta lactam macrolide combination, fluroquinolone mono therapy, beta lactam fluoroquinolone combination therapy, and doxycycline. Combination therapy is preferred for severely affected patients, while monotherapy is suitable for non-ICU patients. Macrolide along with beta lactam combination therapy is the better option for community acquired pneumonia.

Keywords: Pneumonia, Community acquired pneumonia, management, beta lactam macrolide combination therapy

Introduction

Pneumonia refers to the inflammation or infection of lung parenchyma. This results in inflammation of lung air sacs, making breathing difficult due to swelling with liquid or pus. Its causes include bacteria, virus, fungi, and parasite. Symptoms include chest pain, coughing, fever, chills, confusion, headache, muscle pain, and fatigue. There are different classifications of pneumonia such as CAP, HAP, HCAP, ventilator acquired pneumonia, and aspiration pneumonia. Patient is suffering from a community-acquired acute lung tissue infection known as pneumonia[1][2]. Immediate hospitalization is required within 48 hours. Hospital acquired pneumonia occurs when a patient develops lung infection after 48 hours of hospitalization. - Ventilator acquired pneumonia is when a patient acquires pneumonia 48 hours after endotracheal intubation[1]. - Aspiration pneumonia can occur in hospital or community when a bacterium from the mouth contaminates inhaled stomach content[3]. Patients with pneumonia who were recently hospitalized, had hemodialysis, received chemotherapy, or reside in long-term care facilities have healthcare associated pneumonia[4].

Etiology :

Community-acquired pneumonia is caused by bacteria such as Streptococcus pneumoniae, Haemophilus influenzae, Staphylococcus, Klebsiella pneumoniae, Legionella pneumophila, Mycoplasma pneumoniae, Chlamydophila pneumoniae, Chlamydophila psittaci, Coxiella burnetii and viruses such as influenza, parainfluenza, Varicella zoster viruses[2].

Hospital acquired pneumonia is caused by Gram negative bacteria like Pseudomonas aeruginosa, E. coli, Klebsiella spp. and Gram positive bacteria like S. pneumoniae and S. aureus (including MRSA). Less common organisms include Coliforms like Enterobacter spp, Serratia marcescens, Citrobacter

spp, etc. Other pseudomonas and related species such as S. Maltophilia,

L. Pneumophila (Fungi): Candida albicans, aspergillus fumigatus and viruses like Cytomegalovirus and Herpes simplex virus [2].

Epidemiology: The incidence of community acquired pneumonia varies globally and is influenced by geography, season, and population characteristics. India has a significant burden of pneumonia, with high mortality rates in severe cases. Pneumococci play a crucial role in invasive pneumococcal diseases in India. The reported fatality rates for CAP patients range from 14-30%, and 47% for SCAP [6].

Pathophysiology Of Pneumonia:

Pneumonia is a condition caused by the growth and invasion of pathogenic microorganisms in lung parenchyma, leading to the breakdown of respiratory tract defense mechanisms and the production of intraalveolar exudates. The severity and development of pneumonia are influenced by both pathogen and host factors, such as virulence, inoculum size, and loss of protective upper airway reflexes. Although particulate material and microbes in the upper respiratory tract can enter the lower airways, the lungs' defense mechanisms usually keep the lower airways sterile. Host defenses are classified as innate or acquired, and pneumonia indicates a defect in host defenses, exposure to a particularly virulent microorganism, or a large inoculum size. Predisposing factors to respiratory infection include an overall impairment of the immune response or dysfunction of defense mechanisms, such as smoking, COPD, aspiration, or advanced age. HAP-causing pathogens may originate from medical staff, hospital equipment, or fomites. Aspiration from the upper respiratory and digestive tract is the main mechanism associated with pneumonia in the hospital setting. Predisposing factors for aspiration include depressed cough reflexes, altered consciousness, impaired mucociliary escalator system, and immune suppression. Intubation and mechanical ventilation increase the risk of VAP, as the endotracheal tube enables direct entry of bacteria into the lower respiratory tract and interferes with normal host defense mechanisms, becoming a reservoir for pathogenic microorganisms. Colonization and biofilm formation can occur within 12 hours of patient intubation. The oropharynx and stomach are typically colonized first, followed by the lower respiratory tract and the endotracheal tube [7].

Diagnosis:

Pneumonia, a disease associated with considerable morbidity and mortality, has historically been diagnosed using sputum Gram stains and cultures. These conventional methods are characterized by their slow speed, low sensitivity, and limited specificity. However, over the last decade, innovative diagnostic tools have emerged, especially antigen and nucleic acid detection assays. Incorporating pneumococcal antigen detection techniques, in conjunction with biomarkers such as C-reactive protein and procalcitonin, has the potential to improve the precision of diagnosing pneumococcal pneumonia [8]. Accurate diagnosis of pneumonia involves a combination of clinical evaluation, imaging studies, and laboratory tests. Here are the steps typically followed for a precise diagnosis:

Clinical Evaluation: The healthcare provider will assess the patient's symptoms, medical history, and perform a physical examination. Common symptoms of pneumonia include cough, fever, chest pain, shortness of breath, and fatigue.

Chest X-ray: A chest X-ray is often the initial imaging test conducted to assess the lungs for signs of infection, such as consolidation or infiltrates. However, it's important to note that chest X-rays may not always provide a definitive diagnosis of pneumonia, especially in the early stages.

Lung Ultrasound: Lung ultrasound is a non-invasive imaging technique that can be utilized to detect lung abnormalities associated with pneumonia. It has proven to be a dependable tool for diagnosing pneumonia, particularly in the emergency department setting.

Laboratory Tests: Blood tests, such as a complete blood count (CBC) and blood cultures, may be performed to evaluate the severity of infection and identify the causative organism. Sputum culture and analysis may also be carried out to determine the specific pathogen responsible for the pneumonia [9]. In recent times, several inflammatory biomarkers like procalcitonin (PCT), soluble triggering receptor r expressed on myeloid cells-1 (sTREM-1), pro-adrenomedullin (proADM), and presepsin have emerged as relatively precise biomarkers for bacterial

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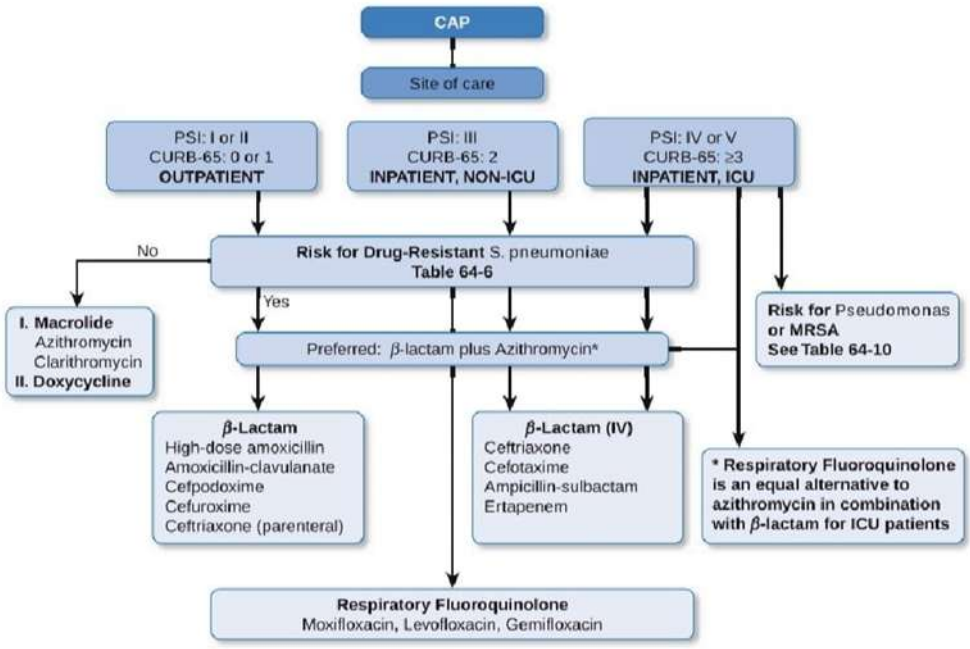
infection. Numerous studies have assessed the efficacy of PCT in diagnosing community-acquired pneumonia (CAP) [10].

Management:



Treatment Options for Community Acquired Pneumonia

Class	Drug Name	Dosing
Macrolides	Azithromycin	500 mg po for 1 day followed by 250 mg po OD for 4 days
	Clarithromycin	250 mg po q12h for 7 days
	Erythromycin	250 mg po qid
Tetracyclines	Doxycycline	100 mg po q12h for 5-7 days
Fluoroquinolones	Levofloxacin	750 mg po OD for 5 days
	Moxifloxacin	400 mg po OD for 7-14 days
Penicillin's	Amoxicillin	1000 mg po qid (plus macrolide or doxycycline) for a minimum of 5 days
	Amoxicillin - clavulanate	2000 mg po bid (plus macrolide or doxycycline) for a minimum of 5 days
Cephalosporins	Cefuroxime	500 mg po bid (plus macrolide or doxycycline) for a minimum of 5 days
	Ceftriaxone	1-2 g IM daily for a minimum of 5 days

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	Cefpodoxime	200 mg q12h for 14 days

Combination Recommended Therapy	Dosage
Antipseudomonal cephalosporin cefepime Ceftazidime	1-2 g IV every 8-12 hours 2 g IV every & hours 500 mg IV every 6 hours or 1g IV every 8hours
Antipseudomonal carbapenem imipenem Doripenem Meropenem Or	500 mg IV every 6-8 hours 1 g IV every 8 hours
B-Lactam/B-Lactamase inhibitor piperacillin-tazobactam (Plus)	4.5 g IV every 6 hours
Antipseudomonal fluoroquinolone Ciprofloxacin Levofloxacin Or	400 mg IV every 8 hours 750 mg IV every 24 hours
Aminoglycoside Amikacin Gentamicin Tobramycin (Plus) Linezolid Vancomycin Azithromycin	15-20 mg/kg IV every 24 hours 5-7 mg/kg IV every 24 hours 5-7 mg/kg IV every 24 hours 600 mg/kg every 12 hours 15 mg every 12 hours 500 mg IV every 24 hours

Beta lactam monotherapy vs Beta lactam macrolide combination

A trial was conducted to test a Beta lactam's non-inferiority compared to a combination of Beta lactam and macrolide in treating community acquired pneumonia. The trial showed that Beta lactam monotherapy delayed clinical stability compared to the combination for patients with atypical pathogens and even legionella. Additionally, the combination therapy was found to be more effective for patients with higher severity of pneumonia [15]. For patients hospitalized with severe pneumonia, the recommended treatment is a combination therapy of beta-lactam and macrolide antibiotics, while mild-to-moderate pneumonia is typically treated with beta-lactam antibiotics alone [16]. In cases of severe community-acquired pneumonia (CAP), there is observational evidence supporting the notion that using both a beta-lactam and a macrolide in combination therapy may enhance survival rates when compared to antibiotic regimens lacking a macrolide [17].

Fluoroquinolones or Beta lactam plus macrolide vs Beta lactam alone

When comparing the use of Beta lactam alone with the macrolide plus Beta lactam regimen or levofloxacin therapy, fluoroquinolone therapy results in a significantly lower treatment failure rate, with moxifloxacin being the most effective [24]. Incorporating a macrolide into the initial treatment approach for Severe Community-Acquired Pneumonia (SCAP) seems to be equally safe and efficient compared to alternative choices. The introduction of a macrolide medication alongside a beta-lactam/beta-lactamase inhibitor or employing a macrolide independently was indicative of a milder form of the disease [25]. Combining a β-lactam antibiotic with a macrolide demonstrated a reduction

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in mortality rates among patients with pneumococcal community-acquired pneumonia (CAP) and those exhibiting a pronounced systemic inflammatory response. When both of these factors coincided, the combination of β-lactam and macrolide antibiotics exhibited a protective effect against mortality in the comprehensive multivariate analysis [26].

Beta Lactam Plus Macrolides Or Beta Lactam Alone:

Researchers tested if using a combination of Beta lactam and macrolide antibiotics improved survival rates for CAP. They analyzed data from RCTs, interventional and observational studies. Results showed that using macrolide with Beta lactam reduced all-cause mortality, especially in severe cases. The combination treatment was found to be more effective for CAP cases[19]. The prognosis of SCAP patients hospitalized in the ICU was notably enhanced when treated with a combination of β-lactam and macrolides, in contrast to those receiving a non-macrolide-containing β-lactam regimen [20].

Beta Lactam Monotherapy, Beta Lactam Combination Therapy Or Fluoroquinolone's Monotherapy:

CAP patients were treated with Beta lactam monotherapy, Beta lactam combination therapy or fluoroquinolones monotherapy. Non-ICU patients showed no difference in effectiveness between Beta lactam monotherapy and Beta lactam macrolide combination therapy. Fluoroquinolone monotherapy seemed to benefit non-ICU patients less. Beta lactam monotherapy was found to be superior for non-ICU patients in clinical trials[18].

Beta Lactam And Macrolide Combination Therapy Vs Fluoroquinolones Monotherapy:

A study compared extended spectrum Beta lactam and macrolide/fluoroquinolones monotherapy for veterans with severe CAP. The trial found that combination therapy with a Beta lactam and azithromycin is more effective than monotherapy with levofloxacin in increasing survival rates for severely affected patients [21].

Doxycycline Vs Beta Lactam Macrolide Combination:

Limited data exists on the effectiveness of Beta lactam with doxycycline compared to Beta lactam with a macrolide for treating hospitalized patients with non-severe CAP; however, scarce data suggests that a regimen involving doxycycline is similarly effective with a better safety profile, and a sub group analysis showed that clarithromycin resulted in a shorter time to clinical stability but azithromycin had a higher cure rate [22].

Fluoroquinolones Or Beta Lactam Plus Macrolide Vs Beta Lactam Alone:

The effectiveness of Beta lactam & macrolide (BLM) vs Beta lactam & fluoroquinolones (BLFQ) combinations for treating patients with CAP was evaluated, with BLFQ showing higher mortality and less frequent use as empirical treatment for severe CAP, likely due to an increased probability for multi-drug resistant pathogens in patients with suspected pseudomonas aeruginosa CAP [23].

Conclusion:

Beta lactam monotherapy is comparable to beta lactam with macrolide or fluoroquinolone for non-ICU patients. Macrolide with beta lactam is better for severe pneumonia patients. Doxycycline data is limited, but clarithromycin has a shorter time to clinical stability and azithromycin has a higher cure rate. Combination therapy is better for severely affected patients, while monotherapy is suitable for non-ICU patients. Macrolide with beta lactam is the best option for community acquired pneumonia compared to other therapies.

Abbreviations - CAP: Community acquired pneumonia; HAP: Hospital acquired pneumonia; VAP: Ventilator acquired pneumonia; HPAP: Health care associated acquired pneumonia.

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