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A REVIEW ON ROLE OF ANTIBIOTICS IN THE MANAGEMENT OF BACTERIAL PNEUMONIA

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ABSTRACT

Pneumonia is a condition characterized by the acute inflammation of the lung parenchyma, which is caused by a variety of microorganisms, including bacteria, viruses, fungi, and parasites. The utilization of antibiotics often encounters challenges in terms of the multitude oftypes available and the improper dosages administered. Furthermore, prolonged antibiotic usecan escalate the risk of multidrug resistance (MDR) in bacteria. Consequently, it is imperativethat the selection and dosage of antibiotics be appropriate in order to mitigate the rate of bacterial resistance. The escalating prevalence of bacterial resistance serves as an indicator of the failure in treating pneumonia, as the eradication of bacteria should be the ultimate objectivein antibiotic administration, in addition to clinical improvement. The aim of this review of existing literature is to elucidate the rationale behind the administration and selection of empiric antibiotics for pneumonia infections, as well as to outline appropriate antibiotic management and ensure its adequacy, particularly in cases of bacterial pneumonia.

KEYWORDS: Antibiotics, Bacterial pneumonia, Management

INTRODUCTION :

Pneumonia was initially introduced during the period of 370-460 BC by Hippocrates.Investigation on pneumonia has been ongoing for an extended duration and commenced to be extensively conducted in the 1800s. In 1819, a medical practitioner by the name of Renè Laennec elucidated pneumonia based on its clinical and pathological manifestations. Pneumonia is an acute inflammation of the pulmonary parenchyma triggered by diverse microorganisms such as bacteria, viruses, fungi, and parasites. The categorization of pneumonia, based on its clinical and epidemiological aspects, is bifurcated into community- based pneumonia or community-acquired pneumonia (CAP), hospital-acquired pneumonia (HAP), and ventilator-associated pneumonia (VAP)[1,2]. According to data provided by the World Health Organization (WHO), pneumonia ranks among the top five diseases with the highest fatality rate globally. The primary treatment for bacterial pneumonia consists of antibiotics, which serve a supportive and anti-inflammatory role. In this comprehensive analysis of existing literature, the author will specifically address the management of antibioticusage in cases of bacterial pneumonia. The preferred class of antibiotics typically employed is the β-lactam group, encompassing penicillin's, cephalosporins, and various other types. However, it is important to exercise caution and avoid inappropriate dosages or prolonged antibiotic administration, as these factors can contribute to the development of multidrug resistance (MDR) among bacteria. The escalating occurrence of bacterial resistance should beregarded as an indication of the inadequacy of infection treatment. Apart from achieving clinical improvement, the optimal eradication of bacteria is also a paramount objective in the administration of antibiotics[2,3]. Several factors may impede the provision of suitable and rational antibiotic therapy. Firstly, delays in diagnosing and recognizing the risk of bacteria responsible for MDR pneumonia can hinder the process. Additionally, physiological abnormalities associated with critical illness can alter the pharmacokinetics and pharmacodynamics of antibiotics. The purpose of this literature review is to elucidate the rationale behind the administration and selection of empiric antibiotics for pneumonia infections, while also emphasizing the importance of appropriate and adequate antibiotic management, particularly in cases of bacterial pneumonia, in order to enhance patient prognosis.[2,3]

ANTIBIOTICS FOR PNEUMONIA

Antibiotics are frequently employed in various types and inappropriately administered doses, which can lead to an increased risk of bacterial multidrug resistance (MDR). The rising incidence of bacterial resistance should be regarded as an indication of the ineffectiveness of infection treatment. It is crucial to administer antibiotics appropriately, ensuring that they do not induce hypersensitive reactions and possess good solubility to optimize tissue penetration. Additionally, they should not harm the normal microflora in the body, demonstrate bactericidalrather than bacteriostatic properties, and avoid long-term side effects. Furthermore, achieving bactericidal levels in the body swiftly and maintaining them for an extended duration is essential. The primary mechanism of action of antibiotics against bacteria involves the inhibition of growth and the eradication of bacteria. Broad-spectrum antibiotics are effective against numerous species of bacteria, while narrow-spectrum antibiotics target only a few species. Antibiotics such as Beta lactam (Penicillin's, Cephalosporins, and Carbapenems') and the glycopeptide group (vancomycin, bacitracin) hinder peptidoglycan synthesis in bacterial cell walls. Similarly, polymyxin and daptomycin inhibit the synthesis of lipoprotein moleculesin the cell membrane, leading to increased permeability and the leakage of substances from within the cell. In contrast, antibiotics that inhibit bacterial protein synthesis, including aminoglycosides, amikacin, gentamicin, macrolides, and azithromycin, either impede the function of the 30S or 50S ribosomal subunit or form bonds with the 30S ribosomal subunit, ultimately resulting in cell death. Quinolones and Rifampicin interfere with nucleic acid metabolism by inhibiting RNA polymerization and topoisomerase activity. Additionally, certain antibiotics, such as nystatin and amphotericin, alter cell membrane permeability, leading to cell lysis. Concentration-dependent killing occurs when antibiotics exert maximum potency at high levels or in large doses, as observed with aminoglycosides and fluoroquinolones. Lastly, the synthesis of folic acid is inhibited by antibiotics, preventing bacteria from absorbing folic acid and necessitating the production of folic acid from benzoic amino acids

(PABA). Examples of antibiotics that exhibit this mechanism include sulfonamides and trimethoprim.[9]

Cephalosporins

First-generation cephalosporins, such as cefazolin, cefadroxil, cephalexin, cephalothin, cefapirin, and cefradin, exhibit significant activity against gram-positive cocci including pneumonia, streptococci, and staphylococcus. However, they are not effective against methicillin-resistant strains of staphylococci. Nevertheless, new compounds have been developed to combat methicillin-resistant strains of E. coli and Klebsiella pneumoniae, albeit with low activity against Enterobacter sp and Acinetobacter sp. Second-generation cephalosporins, such as cefaclor, cefamandole, cefonicids, cefuroxime, cefprozil, lorakarbef, ceforanid, and cefamycin, possess increased resistance to hydrolysis. They exhibit structural similarity to cefoxitin, cefmetazol, and cefotetan, which are effective against anaerobes. This group displays notable variability in terms of activity, pharmacokinetics, and toxicity. In addition to their efficacy against organisms susceptible to first-generation drugs, they also display activity against gram-negative organisms. Third-generation cephalosporins, such as cefoperazone, cefotaxime, ceftazidime, ceftizoxime, ceftriaxone, cefixime, cefpodoxime proxetyl, cefdinir, cefditoren pivoxil, ceftibuten, and moxalactam, exhibit an expanded range of activity against gram-negative bacteria and possess the ability to penetrate the blood-brain barrier. Ceftriaxone and cefotaxime are particularly effective against nonpenicillin-susceptiblepneumococci and are recommended as empiric therapy for severe infections. Infusion of 1 gram of parenteral cephalosporin intravenously yields serum levels between 60-140 mcg/mL. The half-life and dosing interval of these drugs vary considerably. For instance, ceftriaxone, with a half-life of 7-8 hours, can be administered once daily at a dose of 15-50 mg/kg/day. Lastly, cefepime serves as an example of a fourth-generation cephalosporin.[11,12]

EMPIRICAL ANTIBIOTIC THERAPY

Management of pneumonia cases involves the prompt diagnosis and immediate initiation of appropriate antibiotics. Empiric antibiotic administration refers to the administration of antibiotics prior to determining the causative bacteria, based on the bacterial patterns and antibiotic sensitivity observed at the local hospital. Rational and empirical antibiotic administration entails selecting antibiotics in accordance with the bacterial pattern, antibiotic sensitivity Antibiogram, infection location, dosage, and appropriate route of administration at the earliest opportunity. The goal of empiric antibiotic therapy is to decrease mortality rates and treatment expenses, and it is recommended for infections that may exacerbate the clinical condition or pose a life-threatening risk. Empiric antibiotic administration must take into account the unique characteristics of each individual and is categorized as either emergency orurgency.[13,14]

MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA

Antibiotics should be administered promptly to patients diagnosed with community-acquired pneumonia (CAP) in an outpatient setting. In the case of CAP patients presenting at emergencydepartments (ED), it is imperative to initiate antibiotic treatment within 8 hours of their arrivalin the ER. Administering antibiotics within 4 hours can potentially reduce mortality rates. Additionally, if a patient cannot achieve stabilization and experiences respiratory distress, intensive care unit (ICU) intervention becomes necessary. Patients undergoing antibiotic

treatment should undergo clinical evaluation within the initial 72-hour period to evaluate the efficacy of the treatment and the potential need for a change in antibiotics. When administeringantibiotics, it is crucial to consider epidemiological data regarding bacteria and local antibioticsusceptibility. In cases where there is a clinical improvement, the empiric antibiotic therapy should be continued, but if there is a deterioration in the patient's condition, the antibiotic should be adjusted based on the results of bacterial culture. The guidelines for treating community-acquired pneumonia (CAP) recommend stratifying patients into risk groups and selecting an appropriate empiric antibiotic therapy based on factors such as patterns of bacterial resistance, pharmacokinetics and pharmacodynamics of the drugs, presence of drug allergies, past antibiotic use, side effects of the drugs, local pathogens, and cost. The primary objective of administering antibiotics is to mitigate and eliminate bacterial infections, reduce morbidity and mortality rates, and minimize the development of bacterial resistance[15,16]. According to the guidelines for empirical antibiotic therapy in outpatient CAP patients, as outlined by the PDPI, it is important to inquire about the patient's history of antibiotic use in the preceding three months. If there is no history of prior antibiotic use, the recommended choice of antibiotic therapy is a group of β-lactam drugs, specifically oral third-generation cephalosporins, such ascefixime, with a daily dosage of 400 mg divided into two doses every 12 hours for a duration of 5 to 7 days, unless there is abnormal creatinine clearance, in which case the dosage should be reduced by 50-70%. Table 2,3, presents the empiric antibiotic therapy options for CAP.

Table 2 represents the empiric antibiotic therapy for CAP patients with comorbidities

Without comorbidities , choose one
AMOXICILLIN 1000mg (or) DOXYCYCLINE 100mg (or) MACROLIDES : AZITHROMYCIN 500mg → 250 mg/day(or) CLARITHROMYCIN 500mg

Table 3 represents the empric antibiotic therapy for CAP patients with comorbidities

With comorbidities (Heart diseases, liver diseases, lung diseases , renal diseases) choose one of these
COMBINATION THERAPY: AMOXICILLIN/ CLAVULANATE 500mg + AZITHROMYCIN 500mg / CLARITHROMYCIN 500mg BD +DOXYCYCLINE 100 mg BD
MONOTHERAPY: FLUOROQUINOLONE: LEVOFLOXACIN 750 mg OD (or) MOXIFLOXACIN 400mg OD

MANAGEMENT OF HOSPITAL ACQUIRED PNEUMONIA & VENTILLATOR ASSOCIATED PNEUMONIA:

Initial clinical management of Hospital-Acquired Pneumonia (HAP) encompasses the consideration of the advantageous administration of empirical antibiotics in order to mitigate mortality rates. This approach entails a careful examination of the prolonged utilization of broad-spectrum antibiotics and the emergence of resistance to antimicrobial agents. It is imperative for every healthcare facility to establish and disseminate an antibiogram. These antibiograms are created periodically, based on the local microbial patterns observed during certain time intervals. The initial antibiotic regimen employed is empirical in nature, with a selection of antibiotics capable of providing coverage for 90% of potential causative pathogens,while also taking into account the prevailing antibiogram pattern.[17]

Table 4. Empirical therapy for HAP

Without risk of mortality: Choose one
CEFEPIME 2g IV Q8H PIPERACILLIN /TAZOBACTAM 4.5 g Q6H LEVOFLOXACIN 750 mg IV Q24H IMIPENEM 500mg IV Q6H MEROPENAM 1 gm IV Q6H
With risk of mortality: choose one
CEFEPIME 2g IV Q8H PIPERACILLIN /TAZOBACTAM 4.5 g Q6H LEVOFLOXACIN 750 mg IV Q24H IMIPENEM 500mg IV Q6H AMINOGLYCOSIDES: AMIKACIN 15 -20 mg /kg IV GENTAMICIN 5-7 mg/kg IV And VANCOMYCIN 15 mg /kg IV Every 8-12 hrs

Table 5 Empirical therapy for VAP

AMINOGLYCOSIDES
AMIKACIN 15-20 mg/kg IV Q12H GENTAMICIN 5-7 mg/kg IV Q12H
GRAM POSITIVE WITH MRSA
VANCOMYCIN 15mg/kg 8-12 hours (or) LINEZOLID 600 mg IV Q12H
GRAM NEGATIVE WITH PSEUDOMONAS BETA LACTAM
CEFEIME 2 gm IV Q8H MEROPENAM 1gm IV Q8H PIPERACILLIN /TAZOBACTAM 4.5 gm IV Q6H

SWITCHING THERAPY

Switching therapy is the act of transitioning from parenteral antibiotics to oral antibiotics during the period of initial clinical improvement. This transition is intended to have a similar or equal effectiveness as the antibiotics previously used. As stated by the PDPI, there are specific criteria for making this change in the treatment of CAP. These criteria include stable hemodynamic, improved clinical symptoms, ability to take medication orally, and normal gastrointestinal function. The ideal choice for replacement therapy is an oral antibiotic that hasthe same spectrum of activity as the intravenous antibiotic, and it should be administered onceor twice a day to ensure patient compliance. This transition can be done in three ways: sequentially using the same drug at the same potency, switching over to different drugs but with the same potency, or step down to the same or different drug but with lower potency. Examples of sequential transition include Levofloxacin and Moxifloxacin. An example of switching over is transitioning from intravenous Ceftazidime to oral Ciprofloxacin, while examples of step down include transitioning from intravenous Amoxicillin, Cefuroxime, or Cefotaxime to oral Cefixime. Injectable medication can be administered for a period of 2-3 days, with the safest option being 3 days. On the fourth day, the medication is changed to oral form, allowing the patient to seek outpatient treatment. In the case of CAP patients treated in the

intravenous administration room, they can be switched to oral therapy after 3 days, while patients in the intensive care unit can be given oral therapy after 7 days.[17]

ASSESSMENT OF THE SEVERITY OF THERAPY

The CRP examination may be repeated in patients with community-acquired pneumonia (CAP)on either the third or fourth day of antibiotic therapy. An elevation in CRP levels indicates a heightened likelihood of therapy failure and/or an increased risk of complications. If the CRP value exceeds 10 mg/dl on the fourth day of therapy, the risk of complications is further amplified. Conversely, patients whose CRP levels are below 3 mg/dl on the third day of therapyexperience a diminished risk of complications. Furthermore, individuals whose CRP levels failto decrease by 50% on the fourth day of therapy face a heightened mortality rate within 30 days, an increased likelihood of requiring mechanical ventilation and vasopressor drugs, as well as an elevated risk of pyothorax, a CAP-related complication.

The PCT examination serves as a marker for identifying the etiology of pneumonia and offersa more favourable prognosis compared to other markers, such as CRP and erythrocytesedimentation rate (ESR). A decline in PCT values signifies an improvement in the infection, whereas an increase exceeding 2mg/ml indicates a poor prognosis. PCT can assist clinicians inpredicting the presence of typical bacteria and aid in determining the most suitable empirical antibiotics. In cases where the patient's condition deteriorates and fails to respond to initial therapy, it is imperative to conduct a thorough evaluation to explore potential differential diagnoses. The prognosis of pneumonia worsens if complications, such as lung abscesses and emphysema.[18]

CONCLUSION:

Pneumonia, characterized by acute inflammation of the lung parenchyma, arises from a varietyof microorganisms namely bacteria, viruses, fungi, and parasites. Antibiotics, support, and anti-inflammatories represent the primary therapeutic approach for bacterial pneumonia. However,an erroneous selection of antibiotic type and dosage, as well as prolonged antibiotic usage, canheighten the vulnerability to bacterial multidrug resistance (MDR). The escalating prevalence of bacterial resistance ought to serve as an indicator of ineffectiveness in managing infections since, beyond mere clinical improvement, complete eradication of bacteria remains the ultimateobjective in each antibiotic administration.

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