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Case Report

Antibiotic use Period in Hospitalized Patients with Pneumonia: A Comprehensive Narrative Review

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Abstract

Pneumonia continues to be a serious worldwide health issue, resulting in considerable morbidity and death in adults. This narrative analysis evaluates the ideal length of antibiotic therapy in individuals with community-acquired pneumonia (CACP), hospital-acquired pneumonia (HACP), and ventilator-associated pneumonia (VASP). Present research indicates that less lengthy antimicrobial sessions are superior in both safety and effectiveness compared to longer sessions, particularly in those suffering from mild to moderate community-acquired pneumonia (CACP), aligning with worldwide guideline suggestions. Data are insufficient for the ideal length of antibiotics in patients with HASP, necessitating individualized treatment based on the causal bacteria and clinical outcome. Lower sessions are seen equally efficient as longer ones in managing VACP, except pneumonia induced by non-fermenting Gram-negative bacteria; although, the length must be calibrated to account for potential increased recurrence rates alongside the established advantages of shorter courses. Furthermore, the confirmation of dependable biomarkers or clinical indicators that discern people likely to gain advantages from abbreviated treatment is essential. This review's findings may inform subsequent studies on tailored antibiotic therapy for pneumonia to enhance results for patients

Introduction

Pneumonia is characterized as an acute infection of the lung parenchyma caused by numerous microbes, and its identification relies on distinct medical, imaging, and laboratory parameters and constitutes a primary cause of illness and mortality worldwide. Pneumonia is defined as Community-Acquired Pneumonia (CACP) or Hospital-Acquired Pneumonia (HACP) based on its method of acquisition [1].

CACP is the second most often cited reason for inpatient treatment. Data indicates that CACP raises morbidity, death, and medical costs. Hospital-acquired pneumonia (HACP) is the predominant healthcare-associated illness in adults, accounting for up to 25% of all these illnesses... Globally released information indicates that CACP is a predominant cause of death among healthcare-associated illnesses, correlating with extended hospitalizations and heightened medical costs [2].

The fundamental therapy for pneumonia is the use of antibiotic medicines. An effective antibiotic schedule, such as dosage, drug selection, and time frame, is crucial for achieving the best patient results. Conversely, excessive length and overly wide-spectrum antibiotics can elevate the likelihood of Clostridium difficile infection and antibiotic-related complications due to extended antibacterial contact, thereby contributing to the emergence of multidrug-resistant organisms [3].

Despite existing data advocating for a reduced length of antimicrobial medication in bacterial pneumonia, particularly in cases of simple community-acquired pneumonia, the extended use of antimicrobials persists as a prevalent behavior, hence increasing the hazards linked to excessive antimicrobial treatment. Minimizing the length of antibiotic therapy in pneumonia patients is essential and may be achieved by effective antimicrobial management initiatives [4,5].

Despite the publication of worldwide recommendations for the management of CACP, VASP, and nvCACP, substantial

gaps and debates persist about the optimum duration of antimicrobial therapy. The decrease in treatment time for these three pneumonia variants is significant due to the elevated rates of antibiotic use and the incidence of organisms that are multidrug-resistant. This review provides a comprehensive update on the evidence concerning the duration of administering antibiotics for various types of pneumonia, emphasizing the efficacy and clinical outcomes of shorter versus longer antibiotic courses, to clarify this contentious issue and identify avenues for further enhancement. This review seeks to elucidate the potential advantages and drawbacks of implementing shorter antibiotic regimens in clinical practice, while also providing insights for optimizing pneumonia treatment protocols to improve patient outcomes and confront the escalating issue of antibiotic resistance [6].

Contemporary protocols regarding the length of antibiotic therapy for varieties of pneumonia

Numerous worldwide recommendations address the diagnostic, treatment, and therapeutic considerations about pneumonia in adults. Compliance with existing standards may result in reduced hospitalization duration, less antibiotic resistance, and lowered healthcare expenditures. Given the excessive use of antibiotics resulting from improper prescriptions and extended treatment durations, it is imperative to revise recommendations to favor a more concise antibiotic regimen. Numerous randomized controlled trials (RCTs) have been conducted; nevertheless, further research is required to ascertain the ideal duration of antibiotic treatment [7].

The British Thoracic Society (BTS) guidelines, issued in 2001 and revised in 2004 and 2009, regarding the control of pneumonia in adults, whether in the community or hospital settings and excluding those with preexisting illnesses like immunodeficiency or malignancy, indicate that the course of treatment and optimal length of antimicrobial therapy are contingent upon the degree of severity evaluation of pneumonia. The recommendations indicate that a 7-day antibiotic regimen is indicated for most patients with low- or moderate-severity uncomplicated pneumonia, while a treatment duration of 7 to 10 days is advised for those with high-severity pneumonia. For proven or suspected infections, like Staphylococcus aureus or Gram-negative enteric bacilli, the recommended length of antibiotic treatment may be prolonged to 14 or 21 days. Recent recommendations from the National Institute for Health and Care Excellence (NICE), released in 2019 and largely amended in 2023, recommend a 5-day therapy for all pneumonia varieties, irrespective of magnitude, upon achieving clinical stability [8].

Hospital-acquired pneumonia

The NICE recommendations, released in 2019, advocate for certain antibiotic treatments contingent upon illness intensity and resistance risk. Risk factors for heightened resistance to antibiotics include illnesses emerging after five or more days in a medical facility, severe pulmonary illness or immunosuppression, recent administration of broad-spectrum antibiotics, colonization by multidrug-resistant bacteria, and recent exposure to a healthcare setting before admission. Per these recommendations, in CACP patients with moderate symptoms and a low resistance risk, the first suggested length of antibiotic therapy is 5 days. Upon completion of the 5-day therapy period, it is recommended to reassess the patient and terminate the treatment if clinical stability is attained. Moreover, in patients exhibiting severe symptoms and indications of sepsis, as well as in hospital-acquired pneumonia (CACP) with an elevated risk of resistance or suspected methicillin-resistant Staphylococcus aureus (MRSA), the length of therapy remains ambiguous. Antibiotics should be reassessed after five days [9].

Ventilator-associated pneumonia

The ideal length of antibiotic therapy, as per ATS/IDSA 2016 recommendations, derived from randomized controlled trials and observational research, is 7 days. The 2017 recommendations from ERS/ESICM/ESCMID/ALAT recommend a period of antibiotic therapy for people with VASP of 7 to 8 days. These rules apply to immunocompetent individuals who do not have cystic fibrosis, lung abscess, empyema, or necrotizing pneumonia. This recommendation for a 7–8-day regimen pertains to patients with non-fermenting Gram-negative bacteria (NF-GNB), Acinetobacter spp., and MRSA who have a favorable clinical outcome [10].

Community-acquired pneumonia

The management of CACP in adults revolves around the appropriate duration of antibiotics, in order to decrease antimicrobial resistance of CACP-related pathogens, such as Streptococcus pneumoniae and Staphylococcus aureus [2]. The optimal duration of antimicrobial treatment remains unclear and controversial. However, several randomized controlled trials (RCTs) and observational studies have increasingly focused on comparing the efficacy (as defined by the clinical cure rates, microbiological eradication, and recurrence rates), the safety, and the adverse effects of short- versus long-course antibiotic regimens in adult patients with CACP [11].

Studies regarding the length of antibiotic therapy for hospital-acquired pneumonia

One of the most critical elements of controlling CACP is ascertaining the ideal length of antibiotic medication, which is essential for enhancing healthcare results, reducing side effects, and mitigating the danger of antibiotic resistance. Amidst increasing antimicrobial resistance, new findings indicate that short-course antibiotic therapy for patients with prevalent bacterial infections, such as CACP, may be equally beneficial as prolonged treatment, contingent upon the patient's clinical progress.

Healthcare practitioners often use data from VASP management to treat NVCA-P patients, since there is a paucity of research comparing short *vs.* extended antibiotic regimens for NVCA-P treatment. The initial study was executed by Singh, et al. who incorporated a heterogeneous ICU population comprising patients with suspected VASP and CACP (Clinical Pulmonary Infection Score (CPIS) below seven). Participants were randomized to receive either standard treatment with broad-spectrum antibiotics for 10–14 days or ciprofloxacin monotherapy, which would be discontinued after 3 days if no progression of pulmonary infiltrate was observed and cultures yielded negative results [11].

The death rate was the same across the two groups; however, the limited antibiotic treatment group exhibited a reduced duration of ICU stay and lower overall costs for antimicrobial medication. Moreover, superinfections, infections with multidrug-resistant bacteria, and antibiotic resistance were recorded in markedly fewer individuals who underwent the short-course treatment [12].

The idea of "shorter is better" was examined in two recent retrospective studies that assessed the efficacy of shorter *vs.* longer antibiotic treatment durations for patients with nvCACP.

Research in a UK secondary care context showed that a shorter antibiotic treatment period of ≤ 5 days for CACP was as effective as longer durations of 6–7 days and > 8 days. Furthermore, abbreviated antibiotic treatment was associated with an increased discharge rate and a reduced duration of hospitalization. In this setting, Tan, et al. showed comparable clinical outcomes for patients on short (5–7 days) and extended antibiotic regimens (10–14 days).

The clinical resolution rates were comparable between the two groups, and no significant difference in death rates was seen at 30 days (17% *vs.* 14.5%) and 90 days (20.5% *vs.* 21.5%). Nonetheless, a greater superinfection incidence was recorded in the prolonged-course group compared to the short-course group, with individuals suffering from nvCACP due to NF-GNP demonstrating the greatest superinfection rate. Therefore, it is essential to provide the minimal effective period of antibiotic treatment to mitigate the proliferation of resistant bacteria, while antibiotic de-escalation should occur promptly based on culture findings to avoid the risk of antimicrobial resistance and drug toxicity.

In a retrospective cohort study involving cases of culture-negative hospital-acquired pneumonia (CACP), patients receiving less than 5 days of empirical MRSA antibiotic coverage exhibited comparable 30-day mortality rates to those receiving more than 5 days of anti-MRSA treatment [13].

Although the body of research on the optimal duration of antibiotic treatment for NVCA-P is limited, it appears that shorter antibiotic regimens are as effective as prolonged courses, resulting in lower rates of superinfection, antimicrobial resistance, and drug toxicity, as well as reduced hospital stays and healthcare costs. An antibiotic treatment length of 5–7 days is deemed suitable for NVCA-P, along with worldwide standards.

At present, insufficient data exist to endorse an antibiotic treatment regimen shorter than 5 days. The length must be customized for each patient, considering criteria such as the causative pathogen and clinical response.

The lack of efficient techniques for assessing therapy effectiveness has led to an emphasis on biomarkers. The validation of novel biomarkers is essential, and further research should focus on the therapeutic advantages of integrating biomarker-guided procedures into patient care.

Randomized controlled trials and high-quality research are essential to validate these results and endorse the shorter-course method, addressing the knowledge gaps in the current literature.

Ventilator-associated pneumonia

In the ICU environment, VASP is a significant contributor to morbidity and death among intubated patients, resulting in prolonged ICU stays, extended time to extubation, elevated antibiotic use, and higher healthcare expenditures. The diagnostic efficacy of existing criteria is marked by inconsistency and poor specificity, whilst microbiological cultures are unable to distinguish between colonization and genuine ventilator-associated pneumonia (VASP).

Randomized clinical trials and meta-analyses have examined whether a reduced duration of antibiotics for treating VASP could diminish unnecessary antibiotic exposure along with side effects, without adversely affecting mortality or rates of infection relapse/recurrence. Additional studies have examined the impact of using clinical criteria and/or biomarkers to inform the early cessation of antibiotics in individuals with VASP [14].

Although current guidelines advocate for a 7–8 day antibiotic regimen in uncomplicated ventilator-associated pneumonia (VASP), the appropriate treatment duration for VASP caused by non-fermenting, frequently multidrug-resistant Gram-negative bacteria (such as Pseudomonas spp., Acinetobacter spp., and Stenotrophomonas maltophilia) remains contentious. Another field of inquiry is the efficacy of using clinical and/or biomarker indices, primarily procalcitonin, to inform the timely discontinuation of antibiotics in certain subpopulations. Furthermore, early-onset ventilator-associated pneumonia (VASP), which occurs within 4–5 days of hospitalization, is linked to more beneficial results than late-onset VASP, potentially due to the presence

of more antibiotic-susceptible pathogens and variations in root causes, thereby allowing for a shorter treatment duration when clinical improvement is evident [15].

Duration of treatment for ventilator-associated pneumonia induced by non-fermenting gram-negative bacteria

In 2005, ATS/IDSA recommendations advocated for a short course (7–8 days) of antibiotics instead of the previously suggested extended term (14–21 days) for the treatment of VASP, excluding NF-GNB VASP, based on the results of the PneumoA RCT. In this experiment, researchers observed no difference in mortality and recurrent VASP between the groups receiving short and long antibiotic regimens, whereas antibiotic-free days were more in the short course [16].

The research also indicated an elevated recurrence risk of VASP attributed to NF-GNB in patients given a short course of antibiotics, despite no significant differences in mortality and any secondary endpoints between the two groups. Nonetheless, the methodology used by the researchers to assess the recurrence of VASP has faced criticism, since the short-course group had a greater number of days-at-risk for recurrence (21 *vs.* 14 days). The difference in VASP recurrences was not significant after accounting for days at risk. Furthermore, recurrence was determined only by microbiological criteria; hence, some recorded instances may be ascribed to colonization rather than genuine infection [17].

Conclusion

The examination of current literature, particularly the consolidated findings from randomized controlled trials and meta-analyses, indicates that abbreviated antibiotic regimens may serve as an effective therapeutic alternative for adult patients with pneumonia. Evidence indicates that abbreviated antibiotic regimens can yield clinical outcomes equivalent to those of standard longer courses, encompassing comparable rates of clinical cure, microbiological eradication, and recurrence, while resulting in reduced antibiotic exposure and resistance, fewer adverse effects, enhanced patient compliance, shorter hospitalization durations, and diminished healthcare costs. The rising prevalence of drug-resistant bacteria and fungal diseases, along with the worldwide acknowledgment of antimicrobial resistance as an urgent issue, necessitates the use of shorter antibiotic regimens. The emphasis on the efficacy of abbreviated antibiotic regimens for pneumonia patients and their prevalent use in clinical settings may aid in mitigating this significant concern. The advancement of antimicrobial stewardship programs in this regard, together with the ongoing promotion of the effectiveness and advantages of abbreviated antibiotic courses, is crucial for their use in clinical practice. Subsequently, when the suggestions for abbreviated courses have been communicated and enacted, and the modification in pneumonia treatment time has transpired, a comprehensive review and continuous audit of the practice alterations are necessary to maintain these adjustments.

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