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Review Article

Review of antibiotics therapy in ventilator associated pneumonia

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Abstract. A significant cause of morbidity and mortality was ranked as ventilator associated pneumonia (VAP). Therefore, studies based on evidence-based pharmacotherapy could help in preventing multiple drug resistance and microorganism colonization. Experts suggested an 8 or 14-21 days course of vigilant antibiotics. Therefore, to reduce toxicity and cost, this systematic review aims to investigate updated antibiotic regimens for VAP. Web of Science, PubMed and Google Scholar were searched. New-onset pneumonia that developing more than 48 hours after endotracheal intubation was defined as VAP. Regarding pulmonary recurrent or excess mortality an 8 days course antibiotic therapy showed appropriate. For treatment of resistant pathogens with high minimum inhibitory concentrations, aerosolized antimicrobilas suggested more effective. Monitoring fever, prolcalcitonin values, C-reactive protein and PaO2/FiO(2) should also be considered. In addition report indicated that serum prolcalcitonin reduces the exposure of antibiotics. A study of 100 VAP patients reported that mortality rates were significantly associated with a change in antibiotic therapy. Published result associated with 12 studies included 3571 patients with VAP, confirmed no statistical difference in all-cause mortality between monotherapy and combination therapy, clinical cure, length of stay in ICU or adverse events. Studies comparing tigecycline versus imipenem-cilastatin for clinical cure in the clinically evaluable population showed statistically significant increase in clinical cure for imipenem-cilastatin. There was no statistical difference in all-cause mortality between carbapenem and non-carbapenem therapies or adverse events, but carbapenems were associated with a statistically significant increase in the clinical cure. Treatment strategy in VAP should be considered based on pathogen reports. Vigilant attention to patient clinical status recommended to be advantageous for considering limited spectrum antibiotics.

Keywords: Antibiotics, ventilator, pathogen, pneumonia, pharmacotherapy.

Introduction

Due to increasing in the prevalence of healthcare associated infections, mortality and antibiotic resistance is increasing additionally. Therefore, antibiotics prescription is a key argument to control antibiotic resistance [1]. As an infectious event nosocomial infections (NIs) occur two days after admission without evidnce that the pathogen was already in the incubation phase [2]. Ventilator associated pneumonia as a significant contributor ranked as the first cause of NIs, that needs antibiotic therapy based on the patient's risk of colonisation by an organism with multidrug resistance. It is well known that higher mortality and longer hospital stay associated with inappropriate initial antimicrobial treatment [3, 4]. Publication reported the commonly pathogens that were associated with multiple-drug resistant called acinetobacter baumanii and klebsiella pneumonia that are responsible for 80% of NIs comprising urinary tract infetions, meningitis, pneumonia, wound infections and bacteremia. [5, 6]. Regarding acinetobacter baumanii cefoperazone sulbactam recommended to be useful with further evaluation regarding effectiveness [7]. Regarding carbapenem-resistant K. pneumonia bacterio-phage therapy as an alternative method for respiratory infections, liver abscesses and bacteremia was suggested [8, 9, 10]. With a reported incidence of 4% associated with methicillin-resistant Staphylococcus aureus, in-hospital mortality rate estimated to be 31%, when methicillin-resistant Staphylococcus aureus is the causative pathogen in pneumonia [11]. For patients with ventilator-associated pneumonia (VAP), antibiotic therapy for seven-day course was recommended [12]. Antimicrobial resistance, Clostridiodes dificile infection, allergic raction. QTc prolongation and thrombocytopenia could be a result of inappropriate antibiotic therapy [13]. Therefore, in intensive care unit a major point to control antimicrobial resistance is to reduce the use of antibiotics.[14-17]. This study aims to evaluate different strategy of antibiotic therapy in VAP.

Materials and Methods

We performed an electronic search of the relevant literature with no language restrictions in: PubMed/Medline and Web of science. With searching "Antibiotics Therapy in Ventilator Associated Pneumonia" there were in; (Web of Science 2052 articles, 2023 to 1991 and PubMED 2538

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articles, 2023 to 1990). The risk of bias assessment of the studies and data extraction and analysis of results was carried out by the clinical pharmacist Z.T and doubts in this step were resolved by asking from clinical experts.

Results

The first cause of health care–associated infections, is ventilator associated pneumonia in intensive care unit in which respiratory tract infections are responsible for greater than 50% of antibiotic therapy [18]. Regarding immuno-comprised patients gram negative bacteria are the most commonly isolated pathogens in VAP that needs antibiotic management [19]. World Health Organization ranked acinetobacter baumannii, Pseudomonas aeruginosa, Klebsiella pneumonia, Escerichia coli and Enterobacter spp. as a critical group of pathogens that requires new antibiotics [20]. A recent publication recommended against adding polymyxin B to the high-dose tigecycline regimen in treating pneumonia caused by carbapenem-resistant *K. pneumoniae* and *A. baumannii* [21]. Vasopressor infusion, acid suppression, delayed luminal nutrition and antibiotic administration could affect the proportion of potentially pathogenic microbes and exacerbrate the clinical conditions in patients at intensive care unit [22]. In this situation dysbiosis could be a result of change in gut microbiota due to factors such as nutrition support, the presence of infection, modified gastrointestinal transit and antimicrobial exposure [23]. For prediction of survival, and outcome in those with VAP, measurement of procalcitonin at onset and day 4 of treatment recommended [24]. In this regard, however for the suspicion of sepsis procalcitonin might be superior to c reactive protein, but it should not be used to guide antimicrobial prescription [25, 26].

Regarding many available antibiotics, resistance due to infection with the gram negative opportunistic pathogen Pseudomonas aeruginosa could cause high morbidity and mortality in VAP [27]. Hydrolysis mediated by the production of degrading enzymes, decreased membrane permeability, drug efflux pump, alteration of drug target are the most important factors associated with antibiotic resistance. Against some of the carbapenem-resistant Enterobateriace, especially Klebsiella pneumoniae carba-pnemase producers, ceftazidime-avibactam,imipenem-relebactam and meropenem-vaborbactam reported to have a potent activity. In addition, ceftazidime-avibactam, ceftolozane-tazobactam, imipenem-relabactam and cefide-rocol have potent activity against multidrug-resistant Pseudomonas aeruginosa. [28-30]. Therefore, the site of infection, time of onset and previous length of stay, previous antibiotic therapy, and known multi-resistant organism colonization hould always be considering in association with management of antibiotic therapy [31].

Discussion

Ventilator associated pneumonia as a source of morbidity and mortality, was reported as the most common nosocomial infections in both adults and children stayed at the intensive care unit [32, 33]. Publication predicted that approximately 10 million people could die each year because of antimicrobial resistance by year 2050 [34]. Therefore, in order to control specific patients' conditions, management of antibiotics and dosage adjustments should be based on inter and intraindividual varitions.

Comparing short versus long antibiotic therapy showed different outcome regarding antimicrobial resistance and adverse effects. Associated with different sites of infections and different infections with gram-negative bacilli not generalization can be made [35]. Cefotaxim was reported as a protective antibiotic against wild-type AmpC-producing Enterobacterales [36]. Cell wall synthesis of bacteria could be inhibits by the beta-lactam imipenem [37-38]. For differentiation and detection of pathogens, monitoring of volatile organic compounds concentrations' may indicate emerging pneumonia [39]. Administration of aerosolized amikacin in combination with systemic antimicrobial therapy improving the outcomes of pateints with VAP, resulting effective initial microbial reduction in the sputum, decreases the generation of reactive oxygen species in leukocyte and declines VAP-mediated cell membrane changes of circulating leukocytes [40].

As the most antibiotis poorly penetrating into the lung, therefore combination of cefiderocol and fosfomycin suggested as a useful strategy in patients with VAP caused by carbapenem-resistant Acinetobacter baumannii. However, in this situation intravenous colistin recommended not to be useful [41-42]. With a high rate of recurrence (25-50%) and mortality (14-50%), predicting infection recurrence following procalcitonin guided antibiotic discontinuation in VAP, tracheal secretions and simplified clinical pulmonary infection score could be used [43].

For patients with clinically suspicion of VAP, early administration of in adequate broad spectrum antibiotics is associated with higher morbidity and mortality and the rate of superinfection in those with prolonged course of antibiotic therapy [44]. When the MICs are ≤8 mg/L, for treating nosocomial pneumonia by extended-spectrum β-lactamase-producing *K.pneumoniae*piperacillin/tazobactam could be an effective alternative to carbapenems [45]. For multidrug-resistant Gram-negative bacteria pneumonia, nebulized colistin sulfate as an adjuvant supportive treatment for intravenous antibiotics maybe can improve clinical efficacy and has high safety [46]. Finally, prolonged antibiotics are associated with toxicity, selection for resistant organisms and secondary infections such as Clostridioides difficile colitis [47].

Conclusion

There is need for a novel evidence based antibiotic treatment strategies for patients with VAP, as it is the second leading cause of death associated with nosocomial infections. Regarding to the rate of reported infection due to the inter- and intra-individual variations, achieving a delicate balance for antibiotic therapy recommended. The duration of antibiotic therapy for patients with VAP caused by Pseudomonas aeruginosa needs further attention.

Conflict of Interest

The Authors declare that there is no conflict of interest.

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