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Major publications in the critical care pharmacotherapy literature: January–December 2016

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ABSTRACT

Purpose: To summarize select critical care pharmacotherapy guidelines and studies published in 2016.
Summary: The Critical Care Pharmacotherapy Literature Update (CCPLU) Group screened 31 journals monthly for relevant pharmacotherapy articles and selected 107 articles for review over the course of 2016. Of those included in the monthly CCPLU, three guidelines and seven primary literature studies are reviewed here. The guideline updates included are as follows: hospital-acquired pneumonia and ventilator-associated pneumonia management, sustained neuromuscular blocking agent use, and reversal of antithrombotics in intracranial hemorrhage (ICH). The primary literature summaries evaluate the following: dexmedetomidine for delirium prevention in post-cardiac surgery, dexmedetomidine for delirium management in mechanically ventilated patients, high-dose epoetin alfa after out-of-hospital cardiac arrest, ideal blood pressure targets in ICH, hydrocortisone in severe sepsis, procalcitonin-guided antibiotic de-escalation, and empiric micafungin therapy.
Conclusion: The review provides a synopsis of select pharmacotherapy publications in 2016 applicable to clinical practice.

Contents

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1. Introduction

Critical care clinicians are challenged with the task of staying abreast of the medical literature in order to optimize clinical outcomes for their patients. The question of how to achieve this while attending to a busy practice is crucial with the constantly expanding body of literature. PubMed searches filtered by year using the keywords *critical care* and *intensive care* show a dramatic increase in identified publications from 5446 and 8170 in 2009 to 14,316 and 16,453 in 2016, respectively.

The Clinical Pharmacy and Pharmacology Section's Research Committee within the Society of Critical Care Medicine tasked a working group with creating a monthly publication in 2009 to keep its members abreast of additions to the medical literature in regards to critical care pharmacotherapy. Thus, the Critical Care Pharmacotherapy Literature Update (CCPLU), comprised of critical care pharmacists, commenced with monthly reviews of publications selected from 31 journals based on the Grading of Recommendations, Assessment, Development and Evaluation (GRADE) system to assess quality of evidence and strength of recommendation in addition to relevance to clinical practice [1]. The monthly CCPLU is now nationally distributed electronically to a mailing group as well as via social media networks. One hundred seven articles were reviewed in 2016 with three guidelines and seven primary literature studies chosen based on their GRADE criteria (highly-rated [1A] for primary literature), their potential to change or reinforce current best practices, and an emphasis on pharmacotherapy in critical care practice.

1.1. Kalil et al. Infectious Diseases Society of America/American Thoracic Society Management of adults with hospital-acquired and ventilator-associated pneumonia [2]

This guideline for the diagnosis and treatment of hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) updated the 2005 iteration [3]. The concept of healthcare-associated pneumonia (HCAP) was removed from the discussion in the 2016 guideline, a major change from the 2005 version. The decision to remove HCAP came from increasing evidence that suggests patients with HCAP are not at as high of a risk for multidrug-resistant organisms (MDROs) as previously considered. These guidelines suggest HCAP may be included in the upcoming community-acquired pneumonia guidelines that are anticipated to be released in 2017 and may define new risk factors for MDROs in HCAP.

GRADE methodology was applied to relevant articles published up to November 2015 for guideline inclusion [1]. This is the first version of the HAP and VAP guidelines to use the GRADE methodology.

Notable changes in this update are found in the newly defined risk factors for MDROs for both HAP and VAP (Table 1). These risk factors are to provide guidance in selecting empiric therapy. Other major changes for this update focused on the initial treatment of HAP and VAP. All suspected cases of HAP and VAP should be empirically covered for *S. aureus*, *P. aeruginosa*, and Gram-negative bacilli (HAP, strong recommendation, very low-quality evidence) and VAP (strong recommendation, low-quality evidence). The panel determined these organisms make up the majority of HAP and VAP cases, and inadequate coverage of these organisms can lead to increased mortality. When choosing empiric treatment, a local and preferably intensive care unit (ICU)-specific antibiogram is suggested. To determine the need for empiric coverage of MDROs including methicillin resistant *Staphylococcus aureus* (MRSA) and *P. aeruginosa*, it is recommended to use the defined risk factors for MDROs, severity of illness, and the local prevalence of drug-resistant organisms (Table 2).

The use of aminoglycosides as a secondary agent for the empiric treatment of VAP is not suggested if other agents with sufficient Gram-negative coverage are available for use (weak recommendation, low-quality evidence). This recommendation is supported by evidence from a meta-analysis demonstrating patients treated with or without an aminoglycoside had similar mortality rates, but those treated with an aminoglycoside had a lower clinical response rate [2,4-6]. The panel made this suggestion due to the poor lung penetration of aminoglycosides as well as the increased risk for drug-induced nephrotoxicity and ototoxicity.

Patients with HAP or VAP caused by *P. aeruginosa* should be treated based on microbiological testing. No preferred agent was recommended due to the paucity of data pointing to a desired agent. Due to this lack of data, the use of a local antibiogram may be helpful in determining the best agent for *P. aeruginosa* coverage. Monotherapy is recommended for most patients with HAP or VAP caused by *P. aeruginosa* (strong recommendation, low-quality evidence); however, in patients with *P. aeruginosa* who continue to be in septic shock or at a high risk of death (i.e., mortality risk >25%) after susceptibility results are available, continuation of two antipseudomonal antibiotics is suggested (weak recommendation, very low-quality evidence) [7-11]. This recommendation is controversial as data shows no difference in mortality, treatment failure, ICU and hospital length-of-stay (LOS), duration of mechanical ventilation or the development of resistance in patients receiving monotherapy compared to combination therapy for a HAP or VAP caused by *P. aeruginosa* [7,8]. The panel looked at evidence for patients in septic shock caused by *P. aeruginosa* from sources other than just HAP and VAP. A meta-analysis demonstrated no difference in mortality, but a propensity-matched analysis determined combination therapy was associated with a decreased mortality [9,10]. The panel felt the potential for decreased mortality outweighed the risks and burden of combination therapy.

In patients with HAP or VAP due to extended-spectrum beta-lactamase-producing species, antibiotic therapy should be based on antimicrobial susceptibility as well as patient-specific factors. The panel decided not to recommend an antibiotic regimen due to a lack of evidence identifying a preferable agent or combination of agents.

A preferred antibiotic regimen was suggested for the treatment of HAP or VAP due to susceptible *Acinetobacter* spp. with a carbapenem or ampicillin/sulbactam (weak recommendation, low-quality evidence). If the *Acinetobacter* is only sensitive to polymyxins, intravenous (IV) polymyxin is recommended (strong recommendation, low-quality

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