HHS Public Access

Author manuscript

Pediatr Crit Care Med. Author manuscript; available in PMC 2018 September 01.

Published in final edited form as:

Pediatr Crit Care Med. 2017 September ; 18(9): 903–904. doi:10.1097/PCC.0000000000001261.

How can we optimize antibiotic use in the pediatric intensive care unit?

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Keywords

Sepsis; antibiotic stewardship; antibiotic de-escalation; pediatrics

An estimated 40–80% of pediatric intensive care unit (PICU) patients receive antibiotics and as much as half of that use may be inappropriate [1, 2]. Antibiotic overuse can have deleterious consequences, including drug toxicities, *Clostridium difficile* infections, and antibiotic resistance, the latter of which is a growing public health concern [3]. The need for judicious antibiotic use has been highlighted by several national and international organizations, and as of January 1st, 2017, antimicrobial stewardship is a Joint Commission standard for all hospitals [4]. However, because delays in antibiotic administration or inappropriate antibiotic choice have been associated with increased mortality in patients with sepsis, rapid administration of broad-spectrum antibiotics is recommended in both the 2016 surviving sepsis campaign guidelines, clinical practice parameters for pediatric septic shock, and is now a Centers for Medicare and Medicaid Services (CMS) performance measure for adult hospitals in the United States [5–8]. Recognizing the apparent tension between rapid administration of broad-spectrum antibiotics and judicious antimicrobial use, these guidelines further recommend daily consideration of whether antibiotics can safely be narrowed in spectrum or discontinued altogether. Unfortunately, data informing optimal antibiotic de-escalation strategies, especially in patients with suspected but not culture proven infections, are limited.

To help understand factors that influence duration of antibiotic prescription for critically ill patients, Fontela et al performed a survey of 62 Canadian pediatric intensivists and 37 pediatric infectious diseases physicians [9]. Four clinical scenarios were presented in which a previously healthy child was admitted to the PICU with pneumonia, sepsis, meningitis, or peritonitis and required mechanical ventilation, fluid boluses, and/or inotropes. By day 3 of hospitalization, the patient has markedly improved and respondents were asked to specify the duration of antibiotic therapy they would prescribe if they were the treating physician. Several additional clinical, laboratory, and microbiologic factors were then presented, and respondents were asked to modify their original treatment duration based on each variable.

Potential conflicts of interest: All authors: no conflicts

Copyright form disclosure: Dr. Himebauch does not have any potential conflicts of interest.

The median recommended duration of antibiotic therapy for the original scenarios ranged from 7 days (pneumonia scenario) to 10 days (meningitis scenario), with infectious diseases physicians generally recommending longer durations of therapy than intensivists, though this difference was not statistically significant. Several “core” factors led to extending the antibiotic duration across all scenarios, including illness severity, presence of an immunodeficiency, infant age group, positive bacterial cultures, persistent leukocytosis or elevated C-reactive protein (CRP), and whether the infection was hospital acquired. However, only viral testing resulted in a shorter duration. The authors concluded that decisions surrounding antibiotic discontinuation are complex and that clinicians often lengthen treatment duration based on non-reassuring clinical or laboratory characteristics despite little evidence supporting this practice.

While surveying clinicians regarding current practice patterns is a valuable first step in informing antibiotic de-escalation strategies, this approach has limitations. In all proposed scenarios, bacterial cultures were obtained *after* antibiotic administration, precluding a reliably negative microbiologic culture from being factored into treatment decisions. Given multiple guidelines recommending blood cultures *prior* to initiation of antibiotics, clinicians would (hopefully) most often have this information available and consider it along with other characteristics in making antibiotic treatment decisions. Related, peritonitis and meningitis are relatively infrequent indications for antibiotic use in the PICU relative to other indications, including suspected ventilator-associated infection, which accounts for up to half of antibiotic use [2]. The study findings may therefore not encapsulate the most frequent considerations for antibiotic discontinuation nor the greatest opportunity to safely reduce antibiotic use. Furthermore, and perhaps beyond the scope of this survey, factors influencing transition from broad to narrow spectrum agents were not measured but represent an important opportunity for judicious antibiotic use. Finally, as the authors acknowledge, a survey can only reflect clinicians’ reported practice and preferences, not evaluate the effectiveness of the stated approach. Evidence based guidelines informing optimal antibiotic de-escalation strategies are therefore urgently needed.

Unfortunately, data to inform such guidelines are currently limited. Several biomarkers have been studied as both screening tools to differentiate bacterial infection from other causes of sepsis as well as to guide duration of therapy, of which procalcitonin is perhaps the best studied. A large randomized trial demonstrated shorter durations of antibiotic therapy with lower mortality in adult ICU patients when procalcitonin level was used as a guide for antibiotic discontinuation compared to usual care [10]. However, data on the effectiveness of this approach are conflicting, the optimal cutoff is yet undetermined and variable across studies, and pediatric data are extremely limited [10–12]. Emerging rapid molecular diagnostic techniques hold promise in earlier tailoring of antimicrobial therapy over of traditional methods by more rapidly identifying both the infecting organism as well as antibiotic resistance determinants, allowing earlier prescription of targeted therapy [13]. Screening cultures for methicillin-resistant *Staphylococcus aureus* (MRSA) may be of benefit in identifying patients at low-risk for invasive MRSA infection, which may allow for more judicious initiation or earlier discontinuation of vancomycin therapy [14]. Finally, and perhaps the most immediately available strategy, collaboration between intensivists and infectious diseases consultants and/or antimicrobial stewardship programs is needed to

optimize adherence to existing guidelines for antibiotic treatment choice and duration. Data suggests that such collaboration results in earlier and more effective antibiotic tailoring as well as improved patient outcomes [15].

Both pediatric intensivists and infectious diseases physicians are faced with the challenge of rapidly administering appropriate broad-spectrum antibiotics to critically ill patients with infections while at the same time limiting unnecessary antibiotic exposure in an era of burgeoning antibiotic resistance. Although on the surface these appear to be opposing forces, they are equally important components of effective antimicrobial stewardship in the PICU. Development of collaborative and evidence-based strategies for antibiotic de-escalation, as advocated for by Fontela et al, represent potential ways to integrate these priorities and in doing so, improve outcomes for individual patients as well as slow the emergence of antibiotic resistance. Regulatory organizations mandating bundled sepsis care as well as antibiotic stewardship programs should promote such collaboration between pediatric subspecialists and measure adherence to currently available as well as future guidelines for antibiotic choice, duration, and de-escalation.

Acknowledgments

Funding: This work was funded by the National Institutes of Health [T32HD060550 supporting K.C.]

Dr. Himebauch received support for article research from the NIH. Dr. Chiotos received support for article research from the NIH and Dr. Himebauch has not.

References

1Blinova E, Lau E, Bitnun A, et al. Point prevalence survey of antimicrobial utilization in the cardiac and pediatric critical care unit. Pediatr Crit Care Med. 2013; 14:e280–8. [PubMed: 23823209]

2Fischer JE, Ramser M, Fanconi S. Use of antibiotics in pediatric intensive care and potential savings. Intensive Care Med. 2000; 26:959–66. [PubMed: 10990113]

3Spellberg B, Guidos R, Gilbert D, et al. The epidemic of antibiotic-resistant infections: a call to action for the medical community from the Infectious Diseases Society of America. Clin Infect Dis. 2008; 46:155–64. [PubMed: 18171244]

4APPROVED: New Antimicrobial Stewardship Standard. Jt Comm Perspect. 2016; 36:1–8.

5Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: International Guidelines for Management of Sepsis and Septic Shock: 2016. Crit Care Med. 2017; 45:486–552. [PubMed: 28098591]

6Davis AL, Carcillo JA, Aneja RK, et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. Crit Care Med. 2017; 45:1061–93. [PubMed: 28509730]

7Kumar A, Roberts D, Wood KE, et al. Duration of hypotension before initiation of effective antimicrobial therapy is the critical determinant of survival in human septic shock. Crit Care Med. 2006; 34:1589–96. [PubMed: 16625125]

8Ferrer R, Martin-Loeches I, Phillips G, et al. Empiric antibiotic treatment reduces mortality in severe sepsis and septic shock from the first hour: results from a guideline-based performance improvement program. Crit Care Med. 2014; 42:1749–55. [PubMed: 24717459]

9Fontela PS, Quach C, Karim ME, et al. Determinants of Antibiotic Tailoring in Pediatric Intensive Care: a National Survey. Pediatr Crit Care Med. 2017 *in press*.

10de Jong E, van Oers JA, Beishuizen A, et al. Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial. Lancet Infect Dis. 2016; 16:819–27. [PubMed: 26947523]

11Shehabi Y, Sterba M, Garrett PM, et al. Procalcitonin algorithm in critically ill adults with undifferentiated infection or suspected sepsis. A randomized controlled trial. Am J Respir. Crit Care Med. 2014; 190:1102–10.

12Downes KJ, Weiss SL, Gerber JS, et al. A Pragmatic Biomarker-Driven Algorithm to Guide Antibiotic Use in the Pediatric Intensive Care Unit: The Optimizing Antibiotic Strategies in Sepsis (OASIS) Study. J Pediatric Infect Dis Soc. 2016; 6:134–141.

13Bauer KA, Perez KK, Forrest GN, Goff DA. Review of rapid diagnostic tests used by antimicrobial stewardship programs. Clin Infect Dis. 2014; 59(Suppl 3):S134–45. [PubMed: 25261540]

14Jinno S, Chang S, Donskey CJ. A negative nares screen in combination with absence of clinical risk factors can be used to identify patients with very low likelihood of methicillin-resistant Staphylococcus aureus infection in a Veterans Affairs hospital. Am J Infect Control. 2012; 40:782–6. [PubMed: 22325726]

15Rimawi RH, Mazer MA, Siraj DS, Gooch M, Cook PP. Impact of regular collaboration between infectious diseases and critical care practitioners on antimicrobial utilization and patient outcome. Crit Care Med. 2013; 41:2099–107. [PubMed: 23873275]