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Does enhanced antibiotic de-escalation really have no benefit in the ICU?

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See related research by Trupka et al. https://ccforum.biomedcentral.com/articles/10.1186/s13054-017-1772-4

In a recent issue of *Critical Care*, we read with interest the article by Trupka et al. [1], who investigated the utility of an enhanced antimicrobial de-escalation (EAD) program in mechanically ventilated patients with suspected pneumonia. They found that the EAD program did not affect the rate of antibiotic de-escalation or the duration of antibiotic therapy in intensive care units (ICUs). We are very interested in this research because it includes important findings for the indication of antimicrobial stewardship in ICUs.

However, several issues potentially affecting the results need to be addressed. First, the definition of ventilatorassociated pneumonia (VAP) is unclear. In the study, 35% of the patients were classified as having pathogenpneumonia. Appropriate antibiotic escalation depends on the precise evaluation of targeted microorganisms. Invasive respiratory sampling and quantitative culture may improve antibiotic treatment protocols in patients with VAP. Giantsou et al. [2] demonstrated that VAP patients diagnosed by bronchoalveolar lavage (BAL) were more likely to achieve antibiotic de-escalation than those diagnosed by tracheal aspiration. Further, Raman et al. [3] showed that it was safe to discontinue antibiotic treatment in VAP patients following negative quantitative BAL culture results. Therefore, the sampling and culture methods used for respiratory microorganisms might confound the evaluation of the utility of the EAD program.

Second, the time from initial antibiotic therapy to deescalation was not reported, although the total antibiotic days were similar between the groups. Antimicrobial stewardship programs can reduce the time to deescalation, which may reduce antibiotic resistance and other antibiotic-related adverse events. Carratalà et al. [4] demonstrated that stewardship of the antibiotic treatment in patients with community-acquired pneumonia reduced the time to oral antibiotic conversion, as well as total antibiotic days. Therefore, the time to de-escalation could be an important surrogate for evaluating the usefulness of an EAD program.

Finally, the report lacked information regarding the initial antibiotic therapy regimen. A recent meta-analysis demonstrated that initial inappropriate antibiotic therapy increased the risk of mortality in a hospital setting [5]. Further, if the spectrum of the initial antibiotic was sufficiently specific and narrow, de-escalation was not always necessary, which might affect the rate of de-escalation. Therefore, the initial antibiotic therapy regimen could be associated with the main results of this study.

In conclusion, we believe that provision of additional data by the authors will help us better understand the utility of EAD programs in ICUs.

Author's response

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We thank Ohki and colleagues for their letter regarding our manuscript examining the addition of an enhanced antimicrobial de-escalation (EAD) program to a highintensity daytime staffing model in an academic ICU [1,

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^{6].} Unfortunately, the authors seemed to have failed to appreciate our conclusions. In no way does our study suggest that antibiotic de-escalation is not achievable in the ICU setting. In fact, among all patients eligible for antimicrobial de-escalation, it was achieved in two-thirds of them in both study groups. This is one of the highest numbers for de-escalation in this type of population reported in the medical literature. The EAD program

simply did not increase this percentage in the intervention group. This is likely a reflection of the ICUs in which we carried out this project. All of the ICUs at Barnes-Jewish Hospital are closed units with high-intensity multidisciplinary staffing providing continuous patient care to include clinical pharmacists. There is also a long history of antimicrobial stewardship being practiced within these ICUs [7].

Ohki et al. suggest that the diagnostic approach for establishing the presence of pneumonia could have influenced our results. This is very unlikely given that we employ a robust methodology for achieving this which includes performing routine bronchoalveolar lavage in our intubated patients with suspected pneumonia, as well as utilizing quantitative bacterial cultures and molecular arrays to identify respiratory viruses. We also found no difference in the time to de-escalation of antibiotics between both study groups, which was approximately 2 days after the start of initial therapy. This is simply a function of the time it takes to perform antimicrobial susceptibility testing in our microbiology laboratory. Lastly, antibiotic therapy is protocolized in our ICUs and reviewed by the ICU team including the clinical pharmacists on a daily basis [7]. We care for a high acuity patient population with a high prevalence of antibiotic resistance [8]. It is very unlikely that the initial spectrum of empiric therapy influenced our results.

Abbreviations

BAL: Bronchoalveolar lavage; EAD: Enhanced antimicrobial de-escalation; ICU: Intensive care unit; VAP: Ventilator-associated pneumonia.

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Authors' contributions

SO, SO, and NS conceived the content of the letter and wrote the text. All authors read and approved the final manuscript.

Ethics approval and consent to participate

Not applicable

Consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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References

- Trupka T, Fisher K, Micek ST, Juang P, Kollef MH. Enhanced antimicrobial deescalation for pneumonia in mechanically ventilated patients: a cross-over study. Crit Care. 2017;21:180.
- Giantsou E, Liratzopoulos N, Eframidou E, Panopoulou M, Alepopoulou E, Kartali-Ktenidou S, et al. De-escalation therapy rates are significantly higher by bronchoalveolar lavage than by tracheal aspirate. Intensive Care Med. 2007;33:1533–40.
- Raman K, Nailor MD, Nicolau DP, Aslanzadeh J, Nadeau M, Kuti JL. Early antibiotic discontinuation in patients with clinically suspected ventilatorassociated pneumonia and negative quantitative bronchoscopy cultures. Crit Care Med. 2013;41:1656–63.
- Carratalà J, Garcia-Vidal C, Ortega L, Fernández-Sabé N, Clemente M, Albero G, et al. Effect of a 3-step critical pathway to reduce duration of intravenous antibiotic therapy and length of stay in community-acquired pneumonia: a randomized controlled trial. Arch Inetrn Med. 2012;172:922–8.
- Raman G, Avendano E, Berger S, Menon V. Appropriate initial antibiotic therapy in hospitalized patients with gram-negative infections: systematic review and meta-analysis. BMC Infect Dis. 2015;15:395.
- Ohki S, Ohshimo S, Shime N: Does enhanced antibiotic de-escalation really have no benefit in the ICU? Crit Care. (In press).
- Micek ST, Ward S, Fraser VJ, Kollef MH. A randomized controlled trial of an antibiotic discontinuation policy for clinically suspected ventilator-associated pneumonia. Chest. 2004;125(5):1791–9.
- Guillamet CV, Vazquez R, Noe J, Micek ST, Kollef MH. A cohort study of bacteremic pneumonia: The importance of antibiotic resistance and appropriate initial therapy? Medicine. 2016;95(35):e4708.