Letter to the Editor

Reduction in antimicrobial use among medical intensive care unit patients during a cluster randomized crossover trial of palliative care consultation

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To the Editor—Intensive care units (ICUs) are one of the largest consumers of antimicrobials, with >70% of patients of receiving antimicrobials on a given day.[1] With the continuing emergence of difficult to treat, costly, and deadly multidrug-resistant pathogens, antimicrobial stewardship strategies to reduce antimicrobial use are urgently needed.[2,3] Patients at the end of life are often cared for in ICUs and frequently receive antimicrobials[4] with uncertain benefits.[5]

We recently conducted a cluster randomized crossover trial of early palliative care consultation in our medical ICUs,[6] with the goal of determining the impact of early palliative care interventions on outcomes of medical ICU patients. The purpose of the current investigation was to determine whether palliative-care consultation in our medical ICU resulted in reduced antimicrobial use at the end of life.

Methods

The details of the trial have recently been described.[6] Briefly, the trial was a single-center cluster randomized crossover trial (August 2017–May 2018) at Barnes-Jewish Hospital (1,250 beds). The study included a 6-week washout period halfway through the study, followed by crossing over to intervention or usual care of the 2 medical ICUs. The Washington University School of Medicine Human Studies Committee approved this investigation, and the need for informed consent was waived (Institutional Review Board no. 201707067; ClinicalTrials.gov Identifier: NCT03263143). All patients admitted on weekdays that were ≥18 years of age and at high risk for morbidity and mortality based on predetermined palliative-care screening criteria could be enrolled as long as they did not meet exclusion criteria.[6] Patients in the intervention arm received palliative-care consultation within 48 hours of ICU admission, and the control arm received standard of care with palliative-care consultation at the discretion of the treating physicians.

Collected data included sociodemographic data; medical co-morbidities; laboratory results; changes in resuscitation preferences; length of stay; duration and use of mechanical ventilation,

vasopressors, and antimicrobials; place of discharge; mortality during the hospital stay; and antimicrobial prescriptions at discharge. Days of antimicrobial therapy were calculated by adding the total number of calendar days of each administered antimicrobial agent. Only antimicrobials with antibacterial properties were considered.

The primary outcome of the current investigation was the proportion of patients receiving antimicrobial prescriptions at hospital discharge among those who did and did not change their resuscitation preference. Our secondary outcomes were total duration of inpatient and outpatient antimicrobials. We compared discharge on antimicrobials between groups using the χ^2 test and duration of inpatient antimicrobials using the Mann-Whitney U test. All statistical analyses were performed using SPSS version 25 software (IBM, Armonk, NY).

Results

In the original trial, 242 patients were enrolled, but only 199 were eligible for the primary outcome.[6] Of these patients, only 132 survived to hospital discharge and had not been on suppressive antimicrobials or active treatment for a previous infection at the time of hospital admission. Of 132 patients, 36 patients (27.3%) changed their code status to do not resuscitate/do not intubate. Of the patients that changed their code status, 6 (16.7%) were discharged on antibiotics compared to 36 patients (37.5%) that did not change their code status. For the 23 patients discharged alive to hospice, none was discharged on antimicrobials.

The proportion of patients discharged on antimicrobials was significantly lower among those having a change in code status ($P = .022$) (Table 1). Of the 132 patients, 116 (87.9%) either died within 30 days of hospital discharge or had at least 30 days of available follow-up data. From these 116 patients, there was no significant difference in the proportion discharged on antimicrobials between those that died within 30 days and those that did not ($P = .14$).

Among the cohort of 132 patients, the median total duration of antimicrobial therapy (inpatient plus outpatient) was significantly different ($P = .044$) between the group that changed their code status and those that did not (Table 1). The median duration of inpatient antimicrobials was not statistically different between those that did and did not change their code status (Table 1). Patients discharged on hospice (n = 23) had significantly ($P = .018$) shorter durations of inpatient antimicrobial therapy (median, 5 days;

Table 1. Duration of Antimicrobials Among Patients Who Did and Did Not Change Their Code Status

Variable	Patients Not Changing Code Status (n = 96)	Patients ChangingCode Status (n = 36)	P Value
Discharged on antimicrobials, no. (%)	36 (37.5)	6 (16.7)	.022
Total duration (days) of antimicrobials (inpatient + outpatient), median (IQR)	9 (4.3–22.3)	6.5 (4–12)	.044
Duration (days) of inpatient antimicrobials, median (IQR)	6 (4–12.8)	5 (4–9.5)	NS

Note. IQR, interquartile range; NS, not significant.

interquartile range [IQR], 3–7) than patients not discharged to hospice (n = 109; median, 7 days; IQR, 4–12). When analyzing by randomization arm, we found no statistically significant difference in discharge on antimicrobial therapy (P = .14). However, patients in the control arm of the study were assigned to usual care, in which they could undergo palliative-care consultation.

Discussion

In a cohort of patients enrolled in a randomized controlled trial of early palliative-care consultation, patients who changed their code status were less likely to be discharged on antimicrobials and to receive overall shorter courses of antimicrobials. This difference was primarily driven by patients transitioning to hospice (n = 23) with 0 of 23 patients discharged on antimicrobials, a number substantially lower than in previous studies.[4]

Palliative care consultants help clarify resuscitation preferences and discuss the risks and benefits of many different therapies for patients at the end of life; antimicrobials are among these. Antimicrobials in patients at the end of life are frequently used but with uncertain benefit.[5,7] Our study suggests that early palliative-care consultation, even when not designed as an antimicrobial stewardship intervention, may nonetheless be effective in reducing antimicrobial consumption in patients at the end of life. Antimicrobial stewardship programs should consider engaging palliative-care providers in the development of end-of-life antimicrobial stewardship efforts.

References

1. Vincent JL, Rello J, Marshall J, *et al*. International study of the prevalence and outcomes of infection in intensive care units. *JAMA* 2009;302: 2323–2329.
2. Antibiotic resistance threats in the United States, 2013. Centers for Disease Control and Prevention website. https://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf. Published 2013. Accessed February 12, 2019.
3. Thorpe KE, Joski P, Johnston KJ. Antibiotic-resistant infection treatment costs have doubled since 2002, now exceeding $2 billion annually. *Health Affairs* 2018;37:662–669.
4. Thompson AJ, Silveira MJ, Vitale CA, Malani PN. Antimicrobial use at the end of life among hospitalized patients with advanced cancer. *Am J Hosp Palliat Care* 2012;29:599–603.
5. Reinbolt RE, Shenk AM, White PH, Navari RM. Symptomatic treatment of infections in patients with advanced cancer receiving hospice care. *J Pain Symptom Manage* 2005;30:175–182.
6. Ma J, Chi S, Buettner B, *et al*. Early palliative care consultation in the medical ICU: a cluster randomized crossover trial. *Crit Care Med* 2019 (in review).
7. Rosenberg JH, Albrecht JS, Fromme EK, *et al*. Antimicrobial use for symptom management in patients receiving hospice and palliative care: a systematic review. *J Palliat Med* 2013;16:1568–1574.

A major monoclonal hospital outbreak of NDM-1–producing *Klebsiella pneumoniae* ST340 and the first report of ST2570 in Brazil

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To the Editor—New Delhi metallo-β-lactamase (NDM) is one of the main globally described carbapenemases. It was first reported in 2009 in India.[1] *Providencia rettgeri* was first reported in Brazil in 2013.[2] NDM emergence has been described in Brazil among gram-negative bacteria related to infection or the environment.[3–5] Here, we describe an outbreak of NDM-1–producing *Klebsiella pneumoniae* (KPN) strains ST340 and ST2570 in 50 single isolates from 2 Brazilian hospitals between May 2017 and July 2018 (Figure 1).