Is there still a room for improvement in antimicrobial use in a setting where use of broad-spectrum antibiotics require approval of an infectious diseases physician?

Gökhan Metan MD[1,2] , Ömrüm Uzun MD[2] , Gülçin Telli Dizman MD[1,2], Meliha Çağla Sönmezer MD[2] , Ahmet Çağkan İnkaya MD[2] , Gülşen Hazırolan MD[3], Murat Akova MD[2] and Serhat Ünal MD[1,2]

[1]Infection Control Committee Hacettepe University Hospitals, Ankara, Turkey, [2]Department of Infectious Diseases and Clinical Microbiology, Hacettepe University Faculty of Medicine, Ankara, Turkey and [3]Department of Medical Microbiology, Hacettepe University Faculty of Medicine, Ankara, Turkey

Antimicrobial resistance (AMR) is a growing problem. Prudent use of the antibiotics is important to combat AMR. In Turkey, all broad-spectrum antibiotics have required the approval of an infectious diseases (ID) specialist for reimbursement since 2003. However, the increased workload of ID physicians during the coronavirus disease 2019 (COVID-19) pandemic may have lowered the threshold to use broad-spectrum antibiotics with concerns of inadequate antibacterial coverage in high number of critical cases.

Audit and feedback, a critical element of a successful antimicrobial stewardship (AMS) program,[1] is uncommon in settings where the use of broad-spectrum antibacterial agents require ID specialist approval.[2] Herein, we present the results of a prospective audit and feedback intervention on the consumption of the certain antibiotics that require ID specialist approval before use.

Methods

Hacettepe University Adult and Oncology Hospitals comprise a 1,171-bed, tertiary-care center with 151 intensive care unit (ICU) beds and a 16-bed hematopoietic stem cell transplantation ward. The authorization of carbapenems, ceftazidime, cefepime, piperacillin-tazobactam, polymyxins, quinolones (except oral forms), glycopeptide antibiotics (vancomycin and teicoplanin), daptomycin, and linezolid are restricted to ID specialists. Because of high rates of AMR of the pathogens in hospital-acquired infections at our institution, patients suspescted of infection are provided consultation at the bedside by ID specialists and are followed until the cessation of therapy, resolution of the symptoms, or discharge. A multidisciplinary team led by ID specialists prepared local diagnostic and management guidelines in the hospital database for empirical antibacterial treatment of some common infections such as sepsis, pneumonia, intrabdominal infections, urinary tract infections, and febrile neutropenia.

The audit-and-feedback intervention was performed between April and August 2021, weekly for April and once each month between May and August. The consulting ID team decided on the type of antimicrobial treatment. All ID consultants reviewed the antimicrobial treatment of 5 randomly selected patients from a ward where they were not in charge as a consultant. Antibiotics were assessed in terms

Author for correspondence: Gökhan Metan, Emails: gokhanmetan@gmail.com, gokhanmetan@hacettepe.edu.tr

of documentation of treatment indication, compliance with the local guidelines, obtaining necessary cultures before prescription, and de-escalation of the antibacterial treatment when possible. Feedback was given individually to each consultant and to resident physicians via e-mail as soon as the auditing process was completed.

The consumption rates of carbapenems, piperacillin-tazobactam, polymyxins and glycopeptides (ie, vancomycin and teicoplanin) were measured in days of therapy per 100 patient days (with 95% confidence interval or CI) between April 1, 2021, and August 30, 2021, by using the hospital database. These rates of consumption were compared with the consumption of the same antibiotics between April 1, 2020, and August 30, 2020, prior to the intervention. We also compared the rates of isolation of multidrug-resistant bacteria in bloodstream infections between the 2 periods. Species identification of the bacteria that were isolated in blood culture were performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS). Antibiotic susceptibility tests were conducted and interpreted in accordance with the European Committee on Antimicrobial Susceptibility Testing (EUCAST) break points.[3] The isolates that were nonsusceptible to ≥1 agent in ≥3 antimicrobial categories were defined as multidrug resistant.[4] The mid-*P* exact test or *z* scores were used to compare the statistical difference. OpenEpi (Open-Source Epidemiologic Statistics for Public Health) version 3.01 software (https://www.OpenEpi.com) was used for the analyses. This study was performed as a routine practice of antimicrobial stewardship committee, and publication of the study report was approved by the Hacettepe University Non-Interventional Clinical Research Ethics Board.

Results

In total, 450 courses of antibiotics in 240 patients were reviewed between April 5, 2021, and August 6, 2021. The overall rate of agreement with local guidelines was 89.1% (403 of 450).

Among 408 cases, the required cultures were obtained before the antibacterial treatment in 377 (82.8%). The indication of antibiotics was documented in 409 (85.9%) of 450 cases. De-escalation of antibacterial treatment based on the culture results was performed in 65.4% of 84 antibiotics that were available for this evaluation. The rate of de-escalation of antibacterial treatment based on culture results was 85.7%. The agreement with local guidelines was 77.4% at the first audit, which had increased to 98.1% by the last audit. Documentation of antibiotic indication increased from 66% to 100%. We detected a decrease in the consumption rates of meropenem, imipenem, colistin, tigecycline, and glycopeptides (vancomycin and

Table 1. Incidence Rate of Multidrug-Resistant Bacteria Bloodstream Infections and Consumption Rates of Antibiotics

Variable	Preaudit Period April 1, 2020–August 30, 2020	Audit Period (April 1, 2021–August 30, 2021	
	Isolation Rate in Blood Cultures per 10,000 patient days (95% CI)	Isolation Rate in Blood Cultures per 10,000 patient days (95% CI)	P Value[a]
Isolated bacteria as the causative agent of bloodstream infections			
Methicillin-resistant *Staphylococcus aureus*	0.81 (0.26–1.89)	0.56 (0.15–1.44)	0.60
Ampicilline-resistant *Enteroccoccus* spp	4.86 (3.27–6.93)	5.07 (3.55– 7.02)	0.86
Ceftriaxone-resistant *Klebisella pneumoniae*	6.31 (4.49–8.63)	5.91 (4.26–7.99)	0.76
Carbapenem-resistant *Klebisella pneumoniae*	4.86 (3.27–6.93)	4.64 (3.19–6.52)	0.85
Ceftriaxone-resistant *Escherichia coli*	6.48 (4.62–8.82)	4.64 (3.19–6.52)	0.15
Carbapenem-resistant *Pseudomonas aeruginosa*	1.94 (1.01–3.39)	2.67 (1.61–4.18)	0.39
Multidrug-resistant *Pseudomonas aeruginosa*	1.45 (0.66–2.76)	2.67 (1.61–4.18)	0.13
Carbapenem-resistant *Acinetobacter baumannii*	3.07 (1.85–4.81)	3.66 (2.39–5.36)	0.57
Antibiotics	Consumption Rate per 100 Patient Days (95% CI)	Consumption Rate per 100 Patient Days (95% CI)	P Value[b]
Carbapenems			<.0001
All carbapenems	14.8 (14.49–15.1)	11.93 (11.67–12.18)	
İmipenem and meropenem	14.26 (13.96–14.56)	10.16 (9.92–10.39)	
Meropenem	14.11 (13.82–14.41)	10.1 (9.86–10.34)	
Ertapenem	0.53 (0.48–0.59)	1.76 (1.67–1.86)	
Piperacillin–tazobactam	3.49 (3.34–3.64)	5.5 (5.33–5.68)	<.0001
Colistin and polymyxin B	2.91 (2.77–3.04)	2.45 (2.34–2.57)	.02
Tigecycline	3.56 (3.42–3.71)	2.14 (2.04–2.25)	<.0001
Vancomycin and teicoplanin	7.36 (7.15–7.58)	5.69 (5.52–5.87)	<.0001
Total consumption	32.12 (31.67–32.57)	27.71 (27.32–28.1)	<.0001

[a]Calculated using the mid-*P* exact test.
[b]Calculated using the *z* score.

teicoplanin). The consumption rates of piperacillin-tazobactam and ertapenem increased when the auditing period was compared with the same period in the previous year. The incidence rates of bloodstream infections caused by several multidrug-resistant bacteria were similar in the 2 periods (Table 1).

Discussion

Increased antibacterial consumption and increasing rates of AMR are concerning during COVID-19 pandemic.[5,6] A recent meta-analysis showed that the increases in the antibiotic consumption rates were higher in lower- and middle-income countries than in high-income countries during the COVID-19 pandemic.[7] Meropenem consumption almost doubled in our hospital in 2020 (9.29 per 100 patient days; 95% CI, 9.13–9.45) compared with 2019 (5.61 per 100 patient days; 95% CI, 5.51–5.72), which was the main reason for the audit. These results demonstrate that even a limited audit and feedback can encourage more prudent use of last-resort antibiotics such as meropenem, colistin, and glycopeptides.

Our study had several limitations. We were not able to compare the demographic and clinical characteristics between 2 periods such as underlying comorbid diseases, number of hospitalized patients with COVID-19, and main infectious sites as cofounders.

In conclusion, every antibiotic prescriber, including ID specialists, would benefit from audit and feedback, which should be done by a

trained ASM team. Sufficient human resources should be allocated, and AMS activities should not be ignored during the pandemic.

References

1. Core elements of hospital antibiotic stewardship programs. Centers for Disease Control and Prevention website. https://www.cdc.gov/antibiotic-use/healthcare/pdfs/hospital-core-elements-H.pdf. Published 2019. Accessed November 11, 2021.
2. Ertürk Şengel B, Bilgin H, *et al.* The need for an antibiotic stewardship program in a hospital using a computerized pre-authorization system. *Int J Infect Dis* 2019;82:40–43.
3. The European Committee on Antimicrobial Susceptibility Testing (EUCAST). Clinical break points. EUCAST website. http://www.eucast.org/clinical_breakpoints/. Accessed March 30, 2022.

4. Magiorakos AP, Srinivasan A, Carey RB, *et al.* Multidrug-resistant, extensively drug-resistant and pandrug-resistant bacteria: an international expert proposal for interim standard definitions for acquired resistance. *Clin Microbiol Infect* 2012;18:268–281.

5. Ghosh S, Bornman C, Zafer MM. Antimicrobial resistance threats in the emerging COVID-19 pandemic: Where do we stand? *J Infect Public Health* 2021;14:555–560.

6. Grau S, Hernández S, Echeverría-Esnal D, Almendral A, Ferrer R, Limón E, Horcajada JP; Catalan Infection Control and Antimicrobial Stewardship Program (VINCat-PROA). Antimicrobial consumption among 66 acute-care hospitals in Catalonia: impact of the COVID-19 pandemic. *Antibiotics (Basel)* 2021;10:943.

7. Khan S, Hasan SS, Bond SE, Conway BR, Aldeyab MA. Antimicrobial consumption in patients with COVID-19: a systematic review and meta-analysis. Expert Rev Anti Infect Ther 2021. doi: 10.1080/14787210. 2022.2011719.