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Concise Communication

Impact of antibiotic heterogeneity by periodic antibiotic monitoring and supervision strategy at two units with different prevalences of multidrug-resistant organisms

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Abstract

In an intensive care unit, antibiotic heterogeneity led to an increase in antibiotic heterogeneity index \( (P = .002) \) and a reduction in carbapenem-resistance Enterobacteriaceae incidence \( (P = .04) \). In a general medicine unit with low prevalence of multidrug-resistant organisms, antibiotic heterogeneity index and incidence of multidrug-resistant organisms did not improve.

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Antibiotic heterogeneity is the concept of using a variety of antibiotics for specific clinical indications to improve hospital ecology, resulting in limiting the emergence of multidrug-resistant organisms (MDROs).1 One of the antibiotic heterogeneity strategies is called Periodic Antibiotic Monitoring and Supervision (PAMS). This strategy has been recommended by Asian experts despite limited evidence.2 Using a hospital-wide PAMS strategy, Takesue et al3 changed the recommended classes of antibiotics for various conditions every 3 months according to the calculated antibiotic heterogeneity index. They noted a decrease in the overall incidence of multidrug-resistant gram-negative bacilli (MDR-GNB).3 Another study reported that implementation of PAMS in a noncritical-care surgical unit did not reduce MDR-GNB.4 Because data on PAMS interventions in medical units are limited, we performed a quasi-experimental study to evaluate the role of PAMS in 2 different medical units with different MDR-GNB prevalences.

Methods

From December 1, 2018, through November 30, 2020, at Thammasat University Hospital (TUH), we performed a quasi-experimental study to evaluate the role of PAMS in an intensive care unit (ICU) with a high incidence of MDR-GNB and in a general medicine unit with a low incidence of MDR-GNB. All patients in these units were prospectively followed for the primary and secondary outcomes. The study periods consisted of 1 year before the implementation of PAMS (December 1, 2018, through November 30, 2019) and 1 year after the implementation of PAMS (December 1, 2019, through November 30, 2020). PAMS was conducted by a multidisciplinary antibiotic stewardship program (ASP) team.

During the entire study period, the antibiotic heterogeneity index, defined daily doses (DDD), and antibiotic usage density were prospectively followed by a clinical pharmacist. The antibiotic usage density was defined as the cumulative use of the specific antibiotics class in DDD divided by the cumulative use of the overall antibiotics classes. During the entire study period, the infection prevention interventions to reduce MDR-GNB included hand hygiene, contact precautions, environmental cleaning and disinfection, and weekly admission active surveillance cultures for CRE. The incidence of MDR-GNB was prospectively monitored by the infection prevention team. The prevalences of MDROs (isolates per 1,000 patient days) in the ICU versus the general medical unit were as follows: MDR Pseudomonas aeruginosa (0.29 vs 0.11), MDR Acinetobacter baumannii (3.45 vs 0.26), carbapenem-resistant Enterobacteriaceae (CRE; 2.70 vs 0.08), and extended-spectrum \( \beta \)-lactamase (ESBL)–producing microorganisms (2.94 vs 0). The primary outcome was improvement in the antibiotic heterogeneity index. The secondary outcomes were MDR-GNB incidence, excluding community-onset ESBL–producing microorganisms,5 antibiotics consumption (DDD per 1,000 patient days), 30-day mortality, and length of hospital stay.

During period 2, a clinical pharmacist calculated the monthly percentage of antibiotic usage density for each antibiotics class. The ASP team then regularly contacted the treating physicians in each unit to recommend the antibiotics that had low antibiotic usage density to replace the current antibiotics regimen. However, the final antibiotics decisions were made by the treating physicians.

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Antibiotic usage density was classified into 3 categories based on a previous study. Recommendations for antibiotics switching are summarized in Supplementary Material 1 (online). A modified version of the Peterson index was used to calculate the antibiotic heterogeneity index (Supplementary Material 1 online). The antibiotic heterogeneity index was used as a surrogate marker for achievement of antibiotic heterogeneity. The thresholds for the antibiotic heterogeneity index were chosen to achieve a target value of >0.85. Data collected included patient demographics, primary outcome, and secondary outcomes. This study was approved by the institutional review board.

All analyses were performed using Stata version 16 software (StataCorp, College Station, TX). We used the χ² test to compare categorical variables. Independent t tests were used for continuous data. Time-series analyses were performed to evaluate the antibiotic heterogeneity index and the incidences of MDR-GNB. All P values were 2-tailed; P < .05 was considered statistically significant.

**Results**

In total, we enrolled 1,390 patients in the preimplementation period (period 1) and 1,265 patients in the postimplementation period (period 2). During period 1, there were 2,764 total patient days in the ICU and 5,565 total patient days in the general medicine unit. In period 2, there were 2,802 total patient days in the ICU and 4,756 total patient days in the general medicine unit. The mean age for all study participants was 62 years (SD, 18.2). The most common underlying diseases were hypertension (55.5%) and diabetes mellitus (35.5%). Demographics and baseline characteristics of the study populations were compared during both periods (Table 1).

Using time series analysis, we detected a significant improvement in the antibiotic heterogeneity index in the ICU (coefficient, 0.0155; P = .002) in period 2 compared to period 1, and the antibiotic heterogeneity index in the general medicine unit improved (coefficient, 0.0205; P = .06). In the ICU, a decreasing trend in the incidence of the overall MDR-GNB occurred in period 2 (coefficient, −0.585; P = .11). Notably, we detected a significant reduction in CRE incidence (coefficient, −0.279; P = .04) as well as a reduction in the incidences of other MDR-GNB (Fig. 1). Compared to period 1, in the ICU, the overall DDD (P = .69), length of stay (P = .97), and 30-day mortality (P = .59) did not improve significantly in period 2 (Table 1). In the general medicine unit, the MDR-GNB incidence decreased (coefficient, −0.377;
However, the overall DDD ($P = .36$), length of stay ($P = .47$) and 30-day mortality ($P = .32$) did not significantly decrease (Table 1).

**Discussion**

Our study yielded some notable findings. First, PAMS was implemented successfully in the ICU, which had a high prevalence of MDROs, and it led to a significant reduction in CRE incidence. Second, due to the low prevalence of MDROs in the general medicine unit, PAMS did not lead to significant reductions in overall MDR-GNB incidence. The key to improvement in the antibiotic heterogeneity index may be a high baseline prevalence of MDROs and a variety of antibiotics options, whereas improvement of MDR-GNB incidence may require a longer PAMS period.

In our study, in the ICU, consumption of carbapenems and β-lactam β-lactamase inhibitors (BLBIs) decreased. These findings may explain the overall decreases in MDR-GNB and a significant

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Fig. 1. Antibiotic heterogeneity index, incidence of overall multidrug-resistant organisms (MDROs), and incidence of specific MDROs in both units.
reduction in the CRE incidence in the ICU. We observed decreases in BLBI consumption in both units, which correlated with the reduction of MDR-*A. baumannii* in both units. Compared with previous studies, our findings suggest that antibiotic heterogeneity index implementation may be successful in a medical ICU where the prevalence of MDROs is high and that such a strategy may not be practical in a general medicine unit with a low MDRO prevalence.

Our study has several limitations. First, this study was performed in a university hospital, where the choices of antibiotics were limited by patient insurance. Thus, our findings may not be applicable to hospitals that have a wider antibiotics choices. Second, the sample size and duration of follow-up in the ICU may not have been sufficient to reveal a significant reduction in antibiotics consumption and specific MDR-GNB incidences. Third, we were unable to evaluate the trend for ESBL-producing microorganisms in the general medicine unit because most cases were community-onset ESBLs. Fourth, time series analysis has limitations because it lacks a comparative arm. Finally, during period 2, the number of patients in the general medicine unit decreased by 11% due to the COVID-19 pandemic.

In conclusion, PAMS can be implemented successfully in a medical ICU with a high MDRO prevalence and may lead to a reduction in the incidence of MDR-GNB and CRE. Successful implementation of PAMS may require a wide variety of antibiotics choices, baseline prevalence of MDROs, and a long follow-up durations. Further studies to evaluate the role of PAMS in specific populations (eg, the neutropenic population and the pediatric ICU) are needed.

**Supplementary material.** To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2021.231

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**References**