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Antimicrobial Stewardship and Improved Antibiotic Utilization in the Pediatric Cardiac Intensive Care Unit

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Abstract

Background: We developed a multidisciplinary antimicrobial stewardship team to optimize antimicrobial use within the Pediatric Cardiac Intensive Care Unit. A quality improvement initiative was conducted to decrease unnecessary broad-spectrum antibiotic use by 20%, with sustained change over 12 months. **Methods:** We conducted this quality improvement initiative within a quaternary care center. PDSA cycles focused on antibiotic overuse, provider education, and practice standardization. The primary outcome measure was days of therapy (DOT)/1000 patient days. Process measures included electronic medical record order-set use. Balancing measures focused on alternative antibiotic use, overall mortality, and sepsis-related mortality. Data were analyzed using statistical process control charts. **Results:** A significant and sustained decrease in DOT was observed for vancomycin and meropenem. Vancomycin use decreased from a baseline of 198 DOT to 137 DOT, a 31% reduction. Meropenem use decreased from 103 DOT to 34 DOT, a 67% reduction. These changes were sustained over 24 months. The collective use of gram-negative antibiotics, including meropenem, cefepime, and piperacillin-tazobactam, decreased from a baseline of 323 DOT to 239 DOT, a reduction of 26%. There was no reciprocal increase in cefepime or piperacillin-tazobactam use. Key interventions involved electronic medical record changes, including automatic stop times and empiric antibiotic standardization. All-cause mortality remained unchanged. **Conclusions:** The initiation of a dedicated antimicrobial stewardship initiative resulted in a sustained reduction in meropenem and vancomycin usage. Interventions did not lead to increased utilization of alternative broad-spectrum antimicrobials or increased mortality. Future interventions will target additional broad-spectrum antimicrobials. *(Pediatr Qual Saf 2024;9:e710; doi: 10.1097/pq9.0000000000000710; Published online February 5, 2024.)*

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INTRODUCTION

Antimicrobials are invaluable in caring for critically ill children by effectively treating life-threatening infections and preventing the spread of infectious diseases. In recent years, global attention has been placed on the proper and judicious use of broad-spectrum antimicrobials to minimize patient harm. The unnecessary use of antibiotics can lead to end-organ damage, the development of secondary infections such as *Clostridioides difficile,* antimicrobial resistance, and other adverse events, resulting in a substantial number of annual healthcare visits and increased expenditures.[1–4] Up to 20% of hospitalized patients receiving antibiotics will experience an adverse drug event, many of which are preventable.[3,5] Additionally, the emergence and spread of antimicrobial-resistant organisms continue to pose a significant challenge to global healthcare systems.[6–8]

The Pediatric Cardiac Intensive Care Unit (CICU) represents a unique setting in which broad-spectrum antimicrobials are prevalent due to the complexity and fragility of patients with heart disease. Patients within the CICU are often challenging to diagnose in the acute inflammatory period and have a high mortality risk, leading to variations in clinical practice and increased reflexive use

of antimicrobial agents.[9] However, unnecessary use of broad-spectrum antibiotics contributes to the emergence of resistant organisms and avoidable adverse events, leading to worsening patient outcomes, prolonged hospital stays, and increased healthcare costs.[10–12]

Antimicrobial stewardship programs (ASP) have emerged as a crucial strategy to assist bedside clinicians with reducing unnecessary antimicrobial use while maintaining optimal patient care.[13–16] The rise of ASPs has led to improved antibiotic use, increased guideline compliance, decreased cost of care, and enhanced productivity.[14,15,17,18] Implementing ASPs in the CICU has unique challenges and requires a multidimensional approach, as these patients are medically complex with multiple stakeholders and require a tailored approach to antimicrobial prescribing.[19] We sought to decrease the unnecessary use of broad-spectrum antimicrobials in the CICU through targeted quality improvement (QI) interventions without compromising patient outcomes. This study aimed to reduce the unnecessary use of meropenem and vancomycin by 20% of baseline days of therapy (DOT) with sustained change over time.

METHODS

Setting

This study occurred at Children's Healthcare of Atlanta (CHOA) in Atlanta, Georgia. The CICU at CHOA is a 32-bed tertiary care unit. The CICU receives approximately 1000 admissions annually and is the intensive care unit for the largest pediatric heart center in the Southeast United States. The CICU cares for children with congenital heart disease, provides peri-operative management, and offers extracorporeal membrane oxygenation. CHOA has separate and distinct neonatal and pediatric ICUs for patients without acute cardiac illness. We use Epic software (Epic Systems Corporation) as the EMR throughout our hospital network.

Multidisciplinary Antimicrobial Stewardship Program

We developed a multidisciplinary antimicrobial stewardship team to monitor antimicrobial use in the CICU. The team consisted of two clinical pharmacists, one from within the CICU and the other from the hospital-wide antimicrobial stewardship program, two attending physicians, one specializing in infectious disease and the other in cardiac critical care, and one critical care fellow. The team first reviewed 6 months of baseline antibiotic utilization data specific to the CICU to understand current prescribing patterns and identify areas of concern. Using this information, we developed a key driver diagram to determine targeted interventions (Fig. 1). The stewardship team held regular meetings to monitor progress, elicit feedback, and refine and optimize interventions to reduce unnecessary antibiotic use.

Interventions

Cycle 1: Provider Education, November 2020

Initial interventions focused on CICU provider education on the importance of antimicrobial stewardship. Members of the stewardship team held three education sessions. The first session, Pediatric Grand Rounds, focused on broad principles of antimicrobial stewardship. The following two sessions introduced the CICU antimicrobial stewardship team and shared unit-specific data. Ongoing stewardship work in similar units, such as the neonatal ICU, was also reviewed. As listed below, additional targeted sessions were held with CICU providers, including attending and fellow physicians, advanced practice providers, and support staff, to build consensus regarding future interventions. Finally, the stewardship team provided just-in-time feedback during the study period when variations in treatment were observed, or new providers were being oriented.

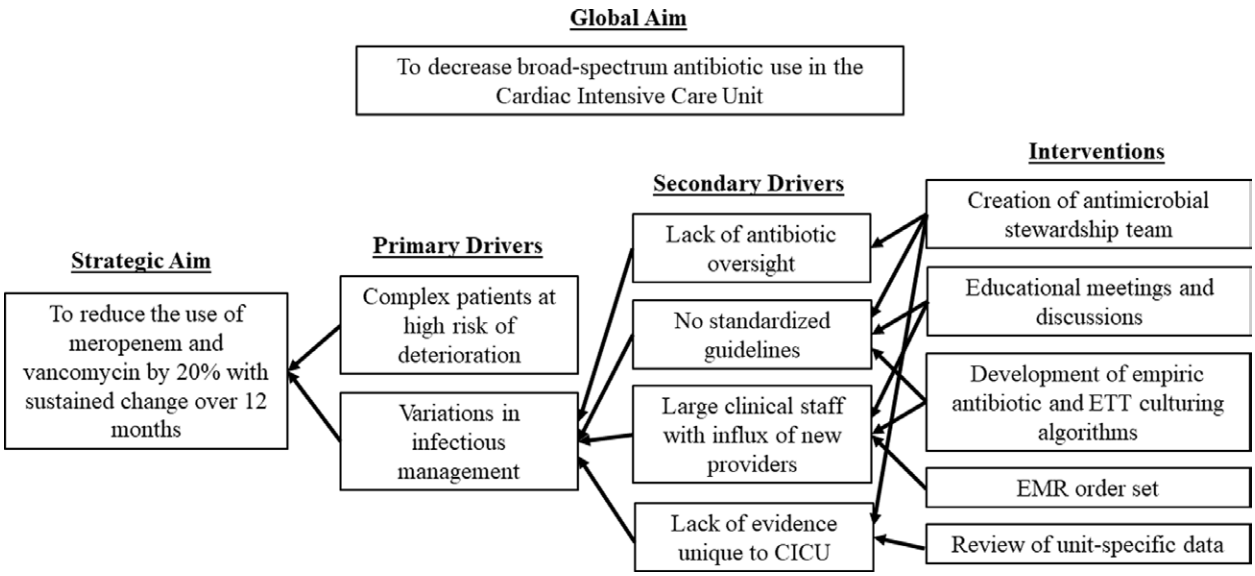

Fig. 1. Key driver diagram of reducing unnecessary broad-spectrum antibiotic use in the pediatric CICU.

Cycle 2: Limiting Empiric Antibiotic Duration, December 2020

The next intervention limited the duration of empiric antibiotics for all patients to 24–36 hours, pending the result of an infectious workup. (**SDC 1,** which displays empiric antibiotic algorithm in the CICU. **http://links.lww.com/PQ9/A534**.) Well-appearing patients admitted from the community received 24 hours of empiric antibiotics. All other patients, including those admitted to the hospital for more than 72 hours and those who were clinically unstable, received 36 hours of empiric antibiotics, pending ongoing workup. To determine this time frame, we reviewed over 500 blood cultures obtained in the CICU and cardiac step-down unit between February 2018 and June 2020. We found that 96% of clinically significant samples were positive by 36 hours. The median time-to-positivity was 13.8 hours. This unit-specific data made us confident that most clinically significant blood cultures from patients undergoing empiric infectious treatment would result before discontinuation of antibiotics. Unstable patients or patients with an identified infectious source, such as a urinary tract infection or pneumonia, were continued on the appropriate antibiotics. We began the implementation of this intervention by informing clinicians during a quarterly divisional QI meeting. Implementation was aided by incorporating automatic stop times in the EMR order-set, discussed below.

Cycle 3: Empiric Antibiotic Algorithm and Order-Set, January 2021

In discussion with the CICU physicians, the antimicrobial stewardship team developed an antibiotic algorithm to standardize treatment choices for empiric antibiotics pending blood culture results (**SDC 1, http://links.lww.com/PQ9/A534**). For patients admitted from the community, antibiotic choice was determined based on age, neonatal versus non-neonatal, and clinical appearance. The empiric antibiotic for hospitalized patients was cefepime monotherapy, with the addition of vancomycin for unstable patients. We selected these antibiotics based on our hospital infectious patterns and antibiogram. Empiric antibiotic duration was also included in the algorithm, as discussed above. To aid in implementation, we transitioned the algorithm to an order-set within the EMR for patients admitted to the hospital for greater than 72 hours, as others received initial workups and antibiotics through the emergency department. The 36-hour antibiotic duration was incorporated into the order-set as an automatic stop time.

Cycle 4: Standardization of Endotracheal Tube Cultures, October 2021

The final intervention focused on practice standardization regarding endotracheal tube (ETT) cultures. Within our unit, ETT cultures may be obtained without clear indication, leading to the identification of non-pathologic organisms and unnecessary antimicrobial therapy. With provider consensus, we created and implemented an algorithm to help bedside providers, including respiratory therapists, recognize the clinical indications for obtaining ETT cultures. (**SDC 2,** which displays endotracheal tube culturing algorithm. **http://links.lww.com/PQ9/A535**.) We held education sessions with these providers to share and implement this algorithm.

Measures and Analysis

The outcome measure utilized for monitoring antibiotic usage was DOT per 1000 patient days (DOT), a measure commonly used by ASPs.[16] We monitored DOT for each antibiotic individually and for broad-spectrum gram-negative antibiotics (ie, cefepime, piperacillin-tazobactam, and meropenem). We collected these data using QlikSense software (Qlik Technologies Inc., King of Prussia, PA). EMR order-set utilization was monitored as a process measure. Balancing measures included all-cause mortality as well as sepsis-related mortality. We used statistical process control charts to review data over time. We reviewed all measures throughout the pre-intervention, intervention, and post-intervention phases from 2018 through 2022.

Ethical Considerations

This QI project did not require review or oversight by the CHOA institutional review board as it was not considered human subjects research per institutional policy.

RESULTS

After implementing interventions focused on provider education and standardization of antimicrobial practices, we achieved a significant and sustained decrease in using meropenem and vancomycin. Meropenem use decreased from a baseline of 103 DOT to 34 DOT, a 67% reduction (**Fig. 2**). The use of vancomycin within the CICU decreased from a baseline of 198 DOT to 137 DOT, a 31% reduction (**Fig. 3**). We sustained this decreased usage for both broad-spectrum antibiotics over 24 months. However, monthly variation occurred. Further, we did not observe an increased use of alternative gram-negative antibiotics, specifically cefepime or piperacillin-tazobactam. Thus, a decreased use of broad-spectrum gram-negative antibiotics, including cefepime, meropenem, and piperacillin-tazobactam, occurred, with an overall reduction of 26% (**Fig. 4**). Special cause variation occurred infrequently throughout the intervention and post-intervention periods for meropenem, vancomycin, and combined gram-negative antibiotics.

After implementing the antibiotic algorithm into the EMR, adoption of the order-set was initially slow and increased steadily (**SDC 3,** which displays provider utilization of empiric antibiotic order-set. **http://links.lww.com/PQ9/A536**). Advanced practice providers and fellow physicians who serve as front-line providers in the CICU utilized the order-set the most.

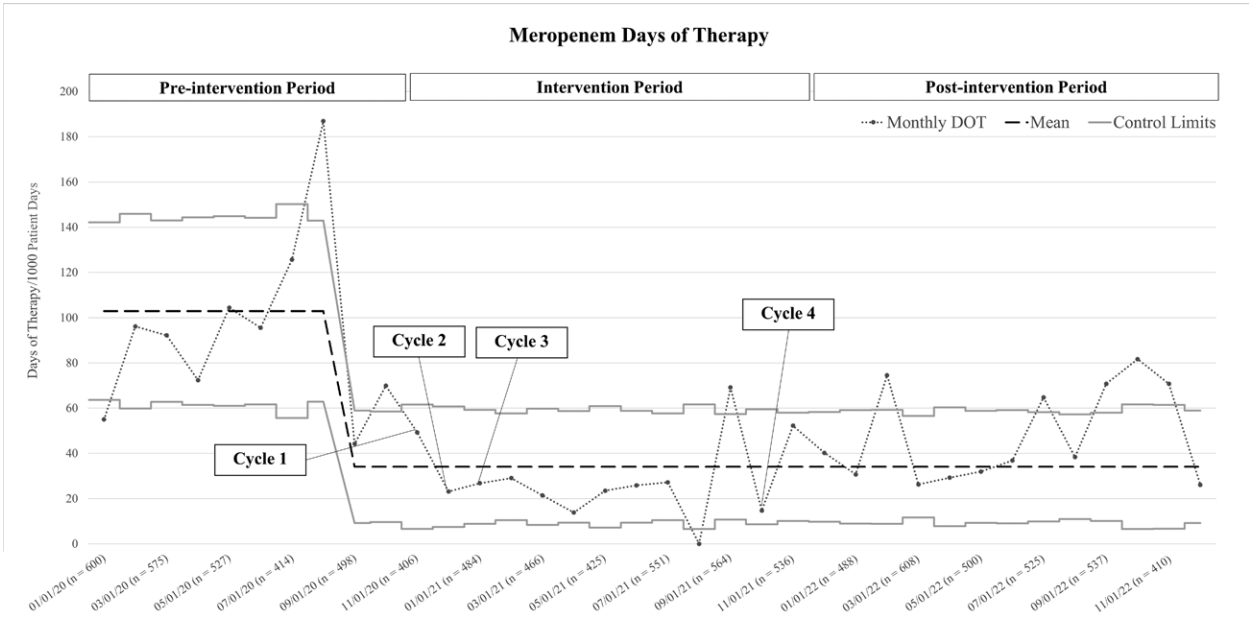

Fig. 2. U-chart displaying the use of meropenem within the CICU.

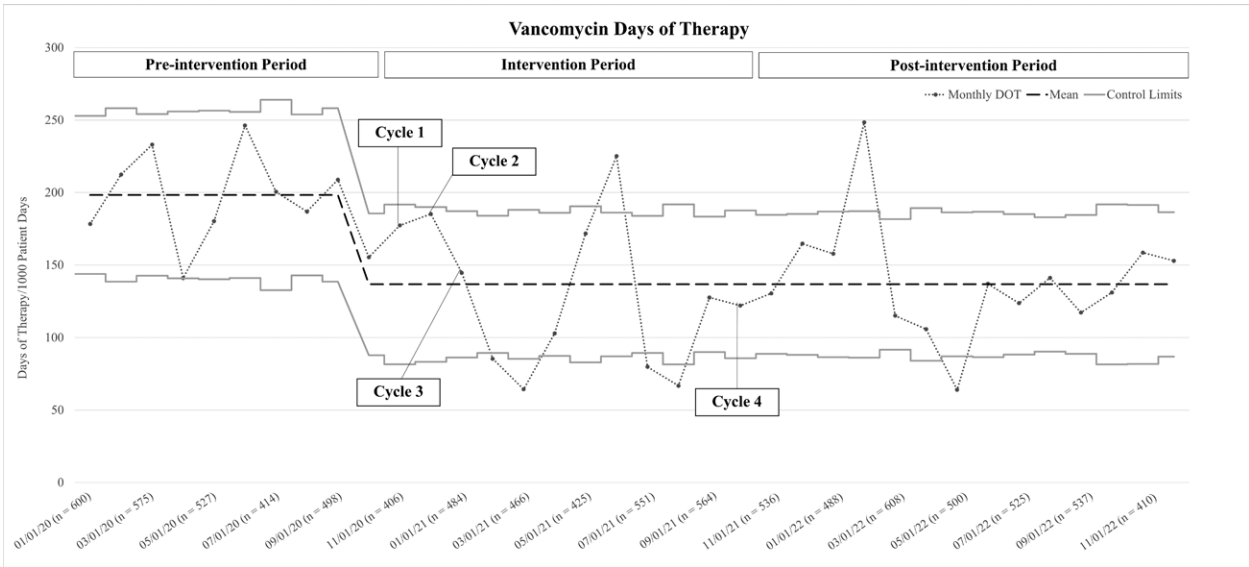

Fig. 3. U-chart displaying the use of vancomycin within the CICU.

The stewardship team monitored balancing measures throughout the intervention period. No significant change was seen in all-cause mortality within the CICU (**Fig. 5**). We observed an increase in sepsis-related mortality in 2021, which returned to the preexisting baseline in 2022 without additional intervention.

DISCUSSION

After implementing the targeted interventions, we decreased the use of meropenem and vancomycin, two broad-spectrum antimicrobials, within the CICU. Minimizing the exposure of medically complex patients to unnecessary antimicrobials decreases the risk of adverse events, such as toxicity, secondary infections, and resistance, thus leading to improved patient outcomes.[4,5] We consider these interventions safe and effective, as we achieved our goal without adversely affecting all-cause mortality. Key interventions included forming a dedicated stewardship team, consensus building around the standardization of empiric antibiotic and culturing practices, and system-based changes within the EMR. Before implementation, we collaborated with key stakeholders from the CICU, including front-line providers, attendings, and pharmacists, to develop all of the stewardship-focused practices.

Previous literature has shown the positive impact of a dedicated ASP on patient outcomes, including duration

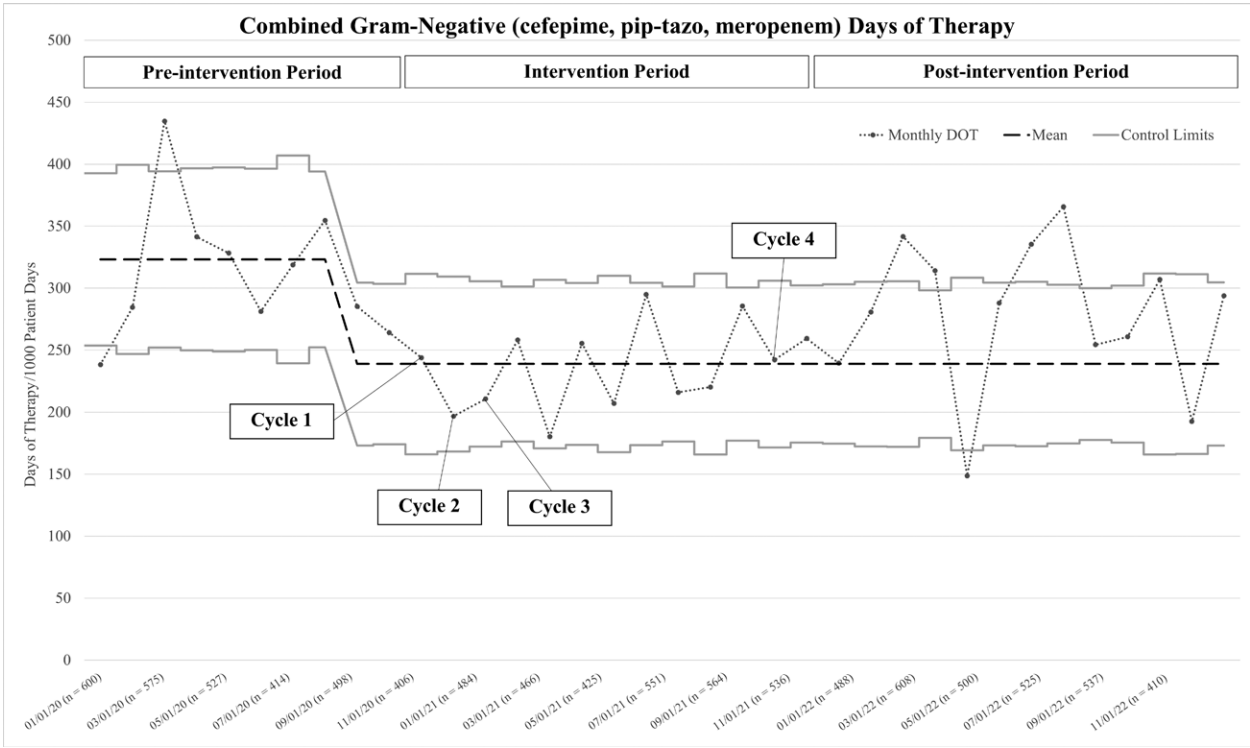

Fig. 4. U-chart displaying the use of gram-negative antibiotics within the CICU. Gram-negative antibiotics included cefepime, piperacillin-tazobactam, and meropenem.

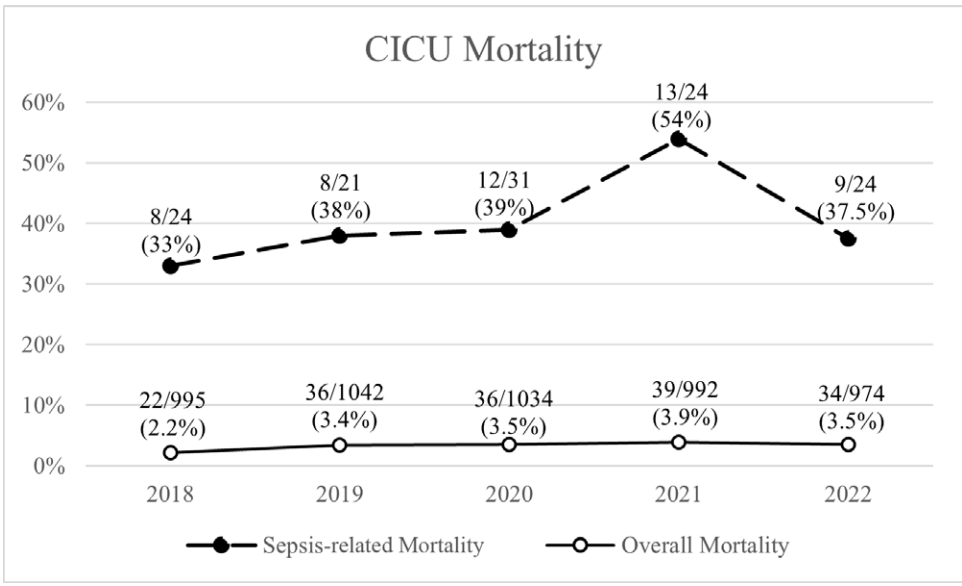

Fig. 5. All-cause and sepsis-related mortality rates in the CICU.

of antimicrobial treatment and length of stay in pediatric patients, including those in the pediatric and neonatal intensive care units.[13–15,18,20,21] Our study supports these previous findings. However, to our knowledge, it is the first to focus on stewardship within the pediatric CICU specifically. Infants and children admitted to the CICU are medically complex and are at high risk of infection, with sepsis reported as one of the leading causes of death in this population.[22] Due to their complexity and fragility, these patients require unique and targeted management of infections.[23] The importance of ongoing collaboration between infectious disease, pharmacists and critical care physicians has been previously documented. We believe developing a dedicated team within the CICU ensured real-time antimicrobial usage review, development of unit-specific guidelines, and ongoing collaboration with front-line providers.

Standardizing the antimicrobial choice and duration for empiric treatment of sepsis was instrumental in decreasing

the use of meropenem and vancomycin. Our empiric antimicrobial algorithm directs therapy based on patient factors, such as age, history, and overall clinical status. While the empiric antibiotics utilized in our algorithm are considered narrower in spectrum than meropenem, we did not observe an increase in mortality. Previous literature supports using empiric antibiotic guidelines to streamline care within the hospital setting, including in intensive care units.[18,21] However, limited studies prove its efficacy or safety within the pediatric CICU.[24] We limited empiric therapy to 36 hours, pending blood culture results. We determined this timeframe using unit-specific time-to-positivity data and studies published in similar patient populations.[25–27] We believe that limiting the duration of empiric antibiotics, in addition to ongoing education and stewardship practices, decreased the use of all monitored antibiotics and prevented an increase in the use of narrower spectrum agents with the implementation of our empiric algorithm. We acknowledge that automatic stop times may lead to unintentional interruptions in antibiotic therapy and require close monitoring by team members.[28]

Diagnostic stewardship is fundamental to antimicrobial stewardship within pediatric intensive care units.[29] Judicious blood culture practices have decreased broad-spectrum antibiotic use in critically ill children.[30] Additionally, Prinzi et al found significant variability in ETT culture rates and increased antibiotic usage associated with ETT culturing.[31] As part of our stewardship initiative, we attempted to standardize the practice of ETT cultures to reduce unnecessary antibiotic use. We developed and implemented an algorithm to support clinical decision-making. Educational initiatives focused on appropriate indications for ETT cultures and targeted clinicians and respiratory therapists. We did not achieve an additional decrease to the centerline with this intervention. However, it likely aided in the sustainment of the new baseline. Ormsby et al found that the implementation of standardized ETT sampling criteria and technique, as well as limiting repeat cultures, led to decreased resource utilization and antibiotic use in children admitted to a medical ICU.[32] Additional research is needed to determine the specific impact of this initiative on broad-spectrum antibiotic use within our cardiac unit.

While consensus building and provider education were key to achieving our aim, we also employed system-based changes to improve adherence. We created and implemented an EMR order-set incorporating the antimicrobial algorithm discussed above. This order-set allowed front-line providers to select pre-determined antibiotics with integrated 36-hour automatic stop times. The order-set contained a link to the algorithm to aid real-time clinical decision-making. As suspected, order-set utilization was variable over time, and ongoing education remains integral to its success, particularly as our unit has a high turnover among the front-line providers. Prior stewardship programs have demonstrated efficacy using similar tactics, such as achieving decreased mortality in patients with sepsis.[33–35]

Special cause variation occurred during multiple months in our pre-intervention, intervention, and post-intervention windows. We believe this occurred in particular patient populations and conditions. For example, patients with endocarditis or ventricular assist device infections received six or more weeks of vancomycin, significantly increasing the overall DOT. Additionally, we treat several chronic patients who develop abdominal pathology that is difficult to culture and treat. These patients often receive prolonged courses of meropenem or piperacillin-tazobactam. The special cause variation did not lead to the rebasing of the centerline.

Limitations

Our study is limited by its single-center, unit-specific nature. We acknowledge that the rate of infection, particularly sepsis, is lower in the cardiac unit compared with other ICUs, such as the NICU and PICU. Thus, antibiotic utilization and improvement strategies may differ at other centers, limiting the generalizability of our study. Additionally, alternative antibiotics to vancomycin, such as linezolid and clindamycin, were not monitored as a balancing measure.

CONCLUSIONS

Targeted QI interventions allowed us to surpass our initial aim of reducing meropenem and vancomycin use by 20% and sustaining those changes over 24 months. Minimizing unnecessary broad-spectrum antibiotics decreased the risk of adverse events, such as end-organ toxicity and the development of resistant infections. Limiting these risks is particularly important in critically ill children with cardiac disease at increased risk of morbidity and mortality. Key interventions included the development of a multidisciplinary stewardship team, practice standardization, and changes within the EMR. The next steps include focused efforts on additional broad-spectrum antimicrobials, such as cefepime and piperacillin-tazobactam.

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