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ORIGINAL ARTICLE

Improving Timely Antibiotic Administration for Pediatric Oncology Patients With Neutropenic Fever Seen in the Emergency Department

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Abstract

Objective: To improve the care for pediatric oncology patients with neutropenic fever who present to the emergency department (ED) by administering appropriate empiric antibiotics within 60 minutes of arrival.

Patients and Methods: We focused on improving the care for pediatric oncology patients at risk of neutropenia who presented to the ED with concern for fever. Our baseline adherence to the administration of empiric antibiotics within 60 minutes for this population was 53% (76/144) from January 1, 2010, to December 21, 2014. During 2015, we reviewed data monthly, finding 73% adherence. We used the Lean methodology to identify the process waste, completed a value-stream map with input from multidisciplinary stakeholders, and convened a root cause analysis to identify causes for delay. The 4 causes were as follows: (1) lack of staff awareness; (2) missing patient information in electronic medical record; (3) practice variation; and 4) lack of clear prioritization of laboratory draws. We initiated Plan-Do-Study-Act cycles to achieve our goal of 80% of patients receiving appropriate empiric antibiotics within 60 minutes of arrival in the ED.

Results: Five Plan-Do-Study-Act cycles were completed, focusing on the following: (1) timely identification of patients by utilizing the electronic medical record to initiate a page to the care team; (2) creation of a streamlined intravascular access process; (3) practice standardization; (4) convenient access to appropriate antibiotics; and (5) care team education. Timely antibiotic administration increased from 73%-95% of patients by 2018. More importantly, the adherence was sustained to greater than 90% through 2021.

Conclusion: A structured and multifaceted approach using quality improvement methodologies can achieve and sustain improved patient care outcomes in the ED.

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Neutropenic fever (NF) in the pediatric oncology patient (POP) is a medical emergency that requires thorough evaluation and treatment, including the timely administration of appropriate empiric antibiotics. Suspected NF in POPs should be considered infectious until proven otherwise, even when typical signs and symptoms of infection are absent. Organisms that are generally thought to have a low infectious potential in healthy patients can have severe consequences for patients with neutropenia.[1] Because of the severity of consequences for this patient population, administration of empiric antibiotics is recommended while evaluating for potential sources for infection and verifying neutropenia.[2] Providing appropriate empiric antibiotics in a timely manner can however raise logistic challenges.

Neutropenic fever in an immunocompromised oncology patient is a cause of morbidity, mortality, and increased health care costs. Evidence-based guidelines from the American Society of Clinical Oncology have recommended that adult patients with suspected NF receive antibiotics within 60

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minutes of arrival.[3] Delaying antibiotics in POPs presenting with suspected NF beyond 60 minutes has been found to increase the odds of patient mortality, pediatric intensive care unit admission, the need for hemodynamic resuscitation, and total length of stay.[4] In 2012, a survey of pediatric oncology centers revealed that 45% of respondents were using time to antibiotics as a quality measure with more than 90% using a standard of less than 60 minutes from the time of presentation to administration in outpatient, Emergency Department (ED), or inpatient setting.[5] In 2017, the International Pediatric Fever and Neutropenia Guideline Panel of the Infectious Disease Society of America recommended the initial antibiotic regimen for children to include an anti-pseudomonal β-lactam, such as cefepime.[1] Based on these national guidelines, the Division of Pediatric Oncology at the study institution established timely administration of empiric administration of a broad-spectrum antibiotic to the standard of care for their POPs.

Other institutions have used quality improvement methods to reduce the door-to-antibiotic time for this patient population with varying degrees of success and sustainment.[6-8] Initiatives at each institution vary based on local resources, interdepartmental relationships, and the unique findings of each gap analysis and root cause process.

To provide the best possible care for POP, we identified a need to improve the timeliness of empiric antibiotic administration for these patients on their presentation to the ED. Recognizing that although other institutions had achieved their goals, replication of specific interventions in our facility would not necessarily yield the same results, we planned to undertake a quality improvement process rather than to implement solutions developed elsewhere.

We aimed to achieve 80% adherence with a door-to-antibiotic time for POPs with suspected NF within 60 minutes of their arrival with appropriate empiric antibiotic selection.

PATIENTS AND METHODS

Context

Our findings are reported using the SQUIRE 2.0 format.[9] As a quality improvement project, this study was exempt per our Mayo Clinc Rochester institutional review board.

Our pediatric ED is colocated with a general ED in a large academic tertiary care center in a small urban area in the midwestern United States. The pediatric ED is a key component of the institution as a level 1 Pediatric Trauma Center. The pediatric ED serves as a referral center for a variety of care centers in the region and specifically provides pediatric cancer care in conjunction with the Division of Pediatric Oncology. On an annual basis, an estimated 18% of children seen in our ED are admitted or observed in the hospital. Between 9:00 AM and 1:00 AM, pediatric patients are seen in a dedicated care area. From 1:00 AM to 9:00 AM, they are seen in the general ED. Our provider team is composed of Pediatric Emergency Medicine and general Emergency Medicine (EM) certified physicians along with resident trainees in Pediatrics, EM, and Family Medicine as well as nurse practitioner and physician assistant students. Emergency Department nursing staff members rotate in different areas of the department and are not solely dedicated to the pediatric area. The ED nursing staff is not required to have prior experience specifically in pediatric care to work in the department; however, they do have ongoing required training with a focus on the care of pediatric patients.

A typical journey through the ED for a POP with NF begins before arrival. Patients/families are instructed to notify the on-call pediatric oncology team if there is a concern for fever, and a prealert call is usually provided to the ED providers to let them know that a potential patient with NF is en route. On arrival, the patient is promptly evaluated and placed in a patient room. Soon after the patient is placed in a room, laboratory studies, including a complete blood cell count with differential and bacterial cultures, are to be drawn with simultaneous establishment of IV access. The preference for IV access is through the utilization of the patient's established indwelling central venous catheter. If problems are encountered with attempts at use of the indwelling catheter, peripheral IV access is then established. After blood cultures are obtained, empiric antibiotics found in the ED medication supply are administered. Results

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of the subsequent workup, including whether the patient is verified to be neutropenic, dictate the ultimate disposition of the patient. Empiric antibiotics are recommended regardless of how ill the patient appeared and were recommended to be administered before the absolute neutrophil count being completed to avoid any potential delays in treatment.

Patients aged less than or equal to 17 years who registered in the ED between January 1, 2010, and December 31, 2021 were included in our measurements if they carried an oncologic diagnosis and had a symptom that included concern for fever. Fever was defined as any temperature measurement of 38 °C or higher. Temperature measurements were included if documented by the clinical or nursing staff in the ED or reported by the parent or patient before arrival in the ED. Patients were excluded if they were transferred from another institution after antibiotics were already administered, received antibiotics before developing fever, or were not followed by our pediatric oncology group. Other immunocompromised/immunosuppressed groups (eg, patients with solid organ transplant) were not included in this project.

We established that we had a gap in care when examining rates of empiric antibiotic administration for POP with possible NF. Between January 2010 and December 2014, there were 144 patients who met the inclusion criteria. Of 144 patients, 76 (53%) received appropriate antibiotics within 60 minutes of arrival. We continued to track the timeliness of administration over subsequent years. A patient registry was created that included patient demographic characteristics as well as time stamps for interventions and medication order data pulled from the electronic medical record (EMR). Of the 41 eligible patients who presented for care to the ED, 73% received antibiotics within 60 minutes. We identified a gap in care that required remediation and a multidisciplinary work group was convened to initiate an improvement project.

Project participants included care team members from pediatric hematology/oncology, pediatric EM, pediatric infusion therapy center, pediatric pharmacy, pediatric infectious diseases, ED nursing, phlebotomy, and a quality nurse specialist (LSH). The team used the Lean quality methodology and principles to identify delays in the process. A value-stream map was assembled to help identify each of the components of an episode of care for a POP with concern for NF. A fishbone diagram was specifically used to facilitate identification of the root causes for delays in care. Environmental/physical, cultural, and individual factors were found to play a role, as well as training/education, process/flow, and availability of equipment and supplies. An example of a specific delay identified by the team included a lack of awareness of all team members when a patient with possible NF was present in the ED.

The multidisciplinary team identified 4 main themes on which to focus, including the following: (1) lack of staff awareness; (2) missing patient information in the EMR; (3) practice variation; and (4) lack of clear prioritization of laboratory draws (Table).

Interventions

Plan-Do-Study-Act Cycle #1. The first Plan-Do-Study-Act (PDSA) cycle focused on timely identification of at-risk patients before and after arrival at the ED. Through a combination of automated alerts in the EMR and direct contact between the pediatric oncologist and the ED physician, patients with concerns for NF were identified more quickly on arrival at the ED. The hospital Admission and Transfer Center was identified as a potential collaborator to help streamline communication between the on-call pediatric oncologist and the ED physician. This also facilitated documentation within the patient's chart for downstream awareness by other team members after the patient's arrival to the ED. The team found that they could utilize an automated process for information from the EMR to trigger a page to the care team assigned to the patient regardless of their location or time of arrival. In addition, visual alerts were displayed on hall-mounted ED track boards to improve awareness of the team staffing the care area. The EMR was updated to allow the triage team to indicate "Neutropenic Fever" as the chief symptom, providing clarity that a patient was high-risk and needed to be seen promptly.

PDSA Cycle #2. The second PDSA cycle focused on streamlining blood draws and

TABLE. Root Causes Identified for Intervention

Theme	Process examples	Solutions
Staff awareness	Poor communication between the ED physician and nursing staff Unreliable alert to patient arrival	Tracking board modified to include unique visual symbol for prompt recognition Pager alert system broadened to include members of IV access team Call system utilized for communication between on-call pediatric oncologist and EM physician regarding patient referral
Missing patient information in the electronic health record	No current weight recorded in the electronic record	Intake personnel education on need for patient weight with entry before rooming
Practice variation	Lack of best treatment algorithm/guideline Differences in perception of urgency by physician Lack of feedback postadmission	Collaboration of team members to develop best practice guideline Dissemination of updated guideline through email and departmental meetings of physicians as well as nursing members Direct feedback provided to EM physicians and nurses regarding metrics for each patient encounter
Priority laboratory draw	No process for identifying laboratory draws that needed to be performed	Group pager system included members of phlebotomy team

ED, emergency department; EM, emergency medicine; IV, intravascular

establishing IV access. Measurements included the number of nursing staff who completed competency training in accessing implanted vascular devices. Specific educational initiatives resulted in establishment of a much larger group of ED nurses who were skilled in the access of implanted vascular devices and peripheral IV placement. These nurses were identified on the track board for the ED and could be called on to establish vascular access more rapidly through reduced failed access attempts. The pages sent to the care team were broadened to include notifications to the nursing team, phlebotomists, and IV infusion nurses. This facilitated greater awareness and more prompt assembly of the multidisciplinary team members needed to care for POPs.

PDSA Cycle #3. The third PDSA cycle focused on standardizing care delivery. Representatives from pediatric hematology/oncology, pediatric EM, pediatric pharmacy, and ED nursing were brought together to discuss barriers to the ordering of laboratory tests and administration of appropriately dosed antibiotics in a timely fashion. Electronic order sets were developed to streamline the ordering process. Up-to-date, timely patient weight measurement early in each ED visit was felt to be a key component in accuracy of antibiotic dosing. A feedback process was created to increase the awareness of the specific times involved in each step of the process for an individual patient. Within 24 hours of the patient's ED visit, all team members involved in a specific patient's care received an email with the important data, including any identified gaps in care. Physician and nursing leaders were able to follow up with the care team both to provide additional education on the process and to solicit information on any barriers they faced in trying to provide optimal care.

PDSA Cycle #4. The fourth PDSA cycle focused on antibiotic ordering and delivery process. The baseline ordering process was mapped out and involved multiple steps, including the identification of need for antibiotics, ordering antibiotics, pharmacy verification of the medication order, and delivery of the antibiotics from the remote pharmacy to the ED. To reduce the steps and delays, preloaded syringes with cefepime were made available in the care area. The immediate availability of premixed antibiotics greatly reduced the amount of time required to complete this step.

PDSA Cycle #5. The fifth PDSA cycle focused specifically on the education of ED staff. Ensuring that all care team members had a solid understanding regarding the "why" behind these interventions was important so that they could prioritize care for these patients. Guideline education was shared at department meetings and nursing competency classes. A specific educational piece was also

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developed as part of the standard onboarding curriculum for new staff.

Control Phase. Ongoing case-by-case performance, root cause evaluation, and ongoing education remain the mainstays of the control phase of this project. We continue to analyze each of the patients regarding each component step in the process as outlined in the fishbone diagram and any reasons for identified delays. For every potential patient with NF, each member of the care team was provided feedback to reinforce the best practices. This ongoing process allowed the team to keep a close watch on any trends that may develop resulting in delays or systems issues that need attention and improvement in near-real time.

Study of the Intervention

With each PDSA cycle, evaluation of the time-to-antibiotic administration was followed. The goal was for all of these high-risk patients to receive an initial dose of antibiotics administered within 60 minutes. This framed the way that data were tracked as an all-or-none, rather than aiming to gradually decrease time to administration or an overall decrease in minutes.

Measures

Our primary measure was the rate of successful appropriate antibiotic administration for patients with fever and neutropenia within 60 minutes. This was measured using time stamps with in the EMR. Although the patients who were found to be neutropenic were the sample used for the primary metric, all POPs with fever were the larger population. Door-to-antibiotic administration was tracked for all POPs with fever, and feedback was provided to all care teams.

RESULTS

Our baseline adherence with timeline antibiotic administration ranged from 20%-80% in the years before the intervention. The sentiment of many members of the providers was that the performance was improving over the time of initial evaluation. However, the performance was not sustained over time with a clear decrease in performance in 2014, which was the year before initiation of the project

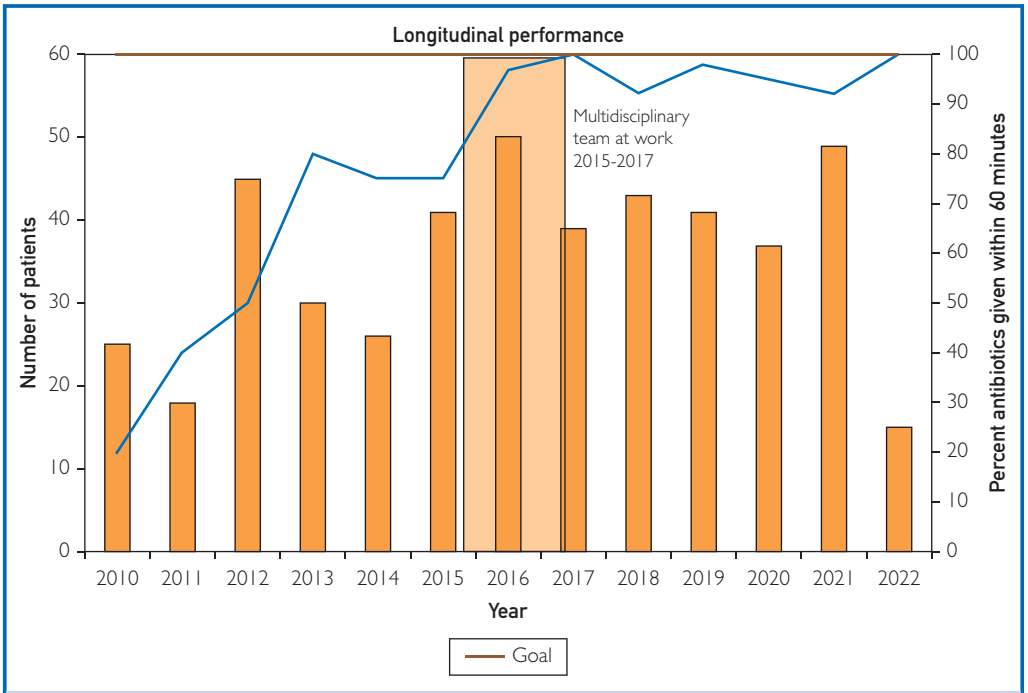

FIGURE 1. Baseline, PDSA, and control phase results. PDSA, Plan-Do-Study-Act.

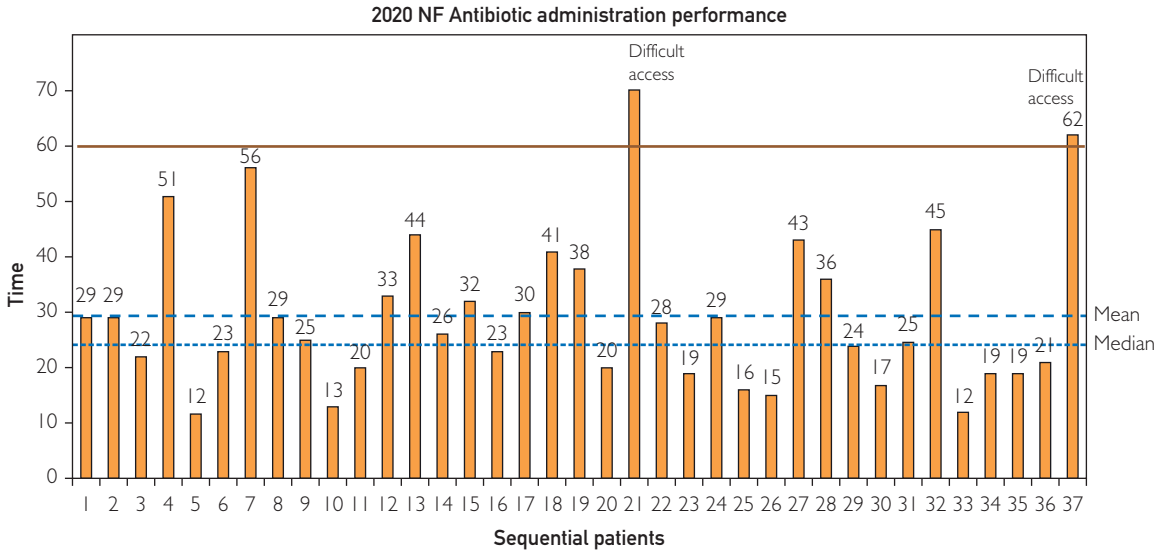

FIGURE 2. Control phase monitoring of sequential patients and time to antibiotic shown with reason for delay. NF, neutropenic fever,

(Figure 1). The improvement team began PDSA cycles in 2015 through 2017, resulting in consistent improvement in performance from an initial 70% adherence to up to 90% and greater for the following years, with ongoing upward movement during the PDSA cycles.

After moving into the control phase in 2017, we were able to maintain performance greater than 90% on a consistent basis, including year-to-date 2022. An example of control phase tracking is demonstrated in Figure 2.

During the control phase, reasons for delay are often because of difficulties with establishment of vascular access. Challenges with vascular access was specified 3 times, delayed laboratory draw 1 time, and delayed rooming 1 time. There was an additional case of delay in care that was felt to be multifactorial. In 2022, year-to-date, there have been no delays in antibiotic administration in this population (Figure 3).

In summary, we found that a structured multidisciplinary approach using quality improvement principles can be applied in a complex ED and yield sustainable high performance for an at-risk pediatric patient population.

CONCLUSION

Summary

Pediatric patients with febrile neutropenia presenting to the ED are relatively less in number, but a high-risk patient group. Using a methodic, quality improvement-based approach, our ED was able to make marked improvements in antibiotic delivery times for these patients and sustain them despite transitioning between EMRs and expected ED staff turnover. Notably, in 2010 only 20% of the patients received antibiotics within 60 minutes of arrival to the ED. Improvements were noted in the subsequent 4 years; however a important percentage of patients continued to not reach the standard of the 1-hour goal to establish vascular access, obtain blood cultures, and receive antibiotics. In 2015, a concerted effort began to formalize efforts to close the remaining gaps.

We attribute our department improvements to multiple factors. We had a multidisciplinary team to provide inputs during the value-stream mapping process. This deliberate step was critical to understand the established workflow and identify gaps in workflow leading to delay in timely response.

Manual methodologies were eliminated through the creation of an automated paging

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system. This process improvement was based on patient demographic characteristics and known laboratory test results and led to more timely identification of these patients on their arrival to the ED. Iterative changes identified through repeated PDSA cycles also allowed us to hone our process. For example, PDSA cycles identified the value of adding additional team members to the pager notification system to improve their awareness of a patient arriving in the ED.

The deliberate engagement of an ED quality specialist led to the creation of an individualized feedback process. Team members involved in each patient care event received specific feedback, including specific data on the times involved from arrival to laboratory order, arrival to antibiotic order, and arrival to administration of antibiotics. This feedback served as reinforcement to the process and highlights the importance of adherence with the guidelines as a department priority.

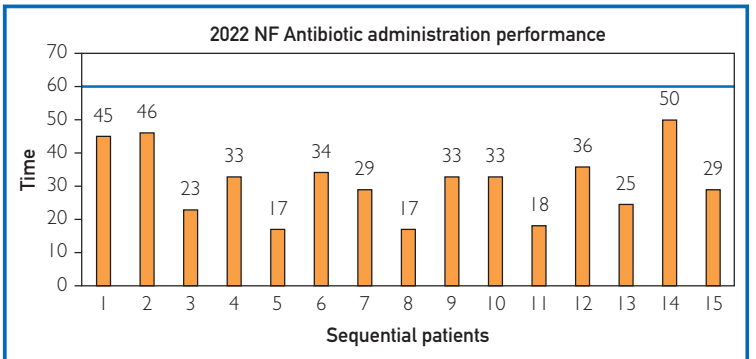

FIGURE 3. Year-to-date 2022 detailed control phase results. NF, neutropenic fever.

Interpretation

Previous quality improvement studies have also attributed their success to involving multiple specialties and disciplines to improve the patient care process.[6,8,10] We were able to identify our institution-specific opportunities for improvement and then gather stakeholder input as to how different opportunities could be approached.

Like Geerlinks et al,[10] we utilized the Lean methodology to be deliberate in our efforts to overcome the barriers to sustained improvements in our practice. However, our practice setting differs from other institutions that have reported on their work caring for POPs with fever. Each ED practice setting has unique aspects that impact care delivery with free-standing EDs being considerably different from EDs embedded within a hospital. Wadhwa et al[11] reported their experience of caring for children admitted with febrile neutropenia episodes from a regional ED as compared with an ED at an institution that provides oncologic care. They reported a delay ($\geq$60 minutes) in antibiotic administration for 80.8% of patients admitted from a regional ED compared with 31.2% admitted from an ED at an institution providing oncologic care.

Pediatric oncology patients at risk of NF require prompt evaluation and care by our emergency care teams. The Lean quality improvement process provided a framework to develop a clear, well organized, and actionable plan to reach our patients in a combined academic adult and pediatric ED setting. Through this process we were able to improve the adherence to expected national timelines and subsequent care of pediatric patients at risk of NF. We increased the percentage of pediatric patients at risk of NF receiving antibiotics within the recommended 60-minute time frame from 73% in 2015 to 95% by 2018 after several PDSA cycles were completed. We have been able to sustain this success over the subsequent 4 years to effectively reach at least 93% of our patients. This quality process, including the specific steps taken, could be translated to other centers to improve time to initial antibiotic administration for POPs with fever.

Limitations

This was done at a single tertiary care academic medical center, with a dedicated pediatric EM practice. The application of the methods outlined may not be applicable to smaller, less-resourced EDs. Additionally, pediatric NF is not a common presenting symptom in our practice setting and the small number of cases being analyzed is also a limitation of our study.

POTENTIAL COMPETING INTERESTS

Dr Heaton has unpaid roles on the Minnesota American College of Emergency Physicians Board of Directors and Epic Specialty Steering Board. Dr Walker was supported by the

American Board of Emergency Medicine. All other authors declare that they have no competing interests.

Abbreviations and Acronyms: **ED,** emergency department; **EM,** emergency medicine; **EMR,** electronic medical record; **NF,** neutropenic fever; **PDSA,** Plan-Do-Study-Act; **POP,** pediatric oncology patient

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