Improving Timeliness of Antibiotic Delivery for Patients With Fever and Suspected Neutropenia in a Pediatric Emergency Department

abstract

OBJECTIVE: There is a high risk for morbidity and mortality in immunocompromised patients with fever if antibiotics are not received in a timely manner. We designed a quality improvement effort geared at reducing the time to antibiotic delivery for this high risk population.

METHODS: The setting was the emergency department in an academic pediatric tertiary care hospital that sees ∼60 000 patients annually. We assembled a multidisciplinary team who set a target of 60 minutes from time of presentation to antibiotic delivery for patients with known neutropenia and 90 minutes for patients with possible neutropenia. Quality improvement methods were used to effect change and evaluate when the targets were not met. Improved communication between providers and patients and timely feedback were implemented.

RESULTS: Mean time to antibiotic delivery in febrile oncology patients with known neutropenic status dropped from 99 minutes in the pre-implementation period to 49 minutes in the postimplementation period, whereas it dropped from 90 minutes to 81 minutes in possibly neutropenic patients. The percentage of patients who met the targets for time to antibiotics rose from 50% to 88.5%.

CONCLUSIONS: A multidisciplinary team approach and standardization of the process of care were effective in reducing the time from arrival to antibiotic delivery for febrile neutropenic patients in the pediatric emergency department. Pediatrics 2012;130:e201–e210
Febrile neutropenia is a potentially life-threatening complication of cancer treatment in children and adolescents. The risk of serious bacterial infection increases when absolute neutrophil count (ANC) is $\leq 500 \text{cells/mm}^3$. Although the causes of fever in immunocompromised patients can be many, the risk of severe bacterial infection makes rapid detection and urgent intervention essential. It is recommended that patients have prompt evaluation for source of infection and rapid initiation of empirical broad spectrum intravenous antibiotics until neutrophil count has sufficiently recovered.

Febrile immunocompromised patients account for $<1\%$ of the total visits at Children’s Hospital Boston Emergency Department (ED). Management of these patients has been guided by a clinical practice guideline (CPG) since 1996. The guideline specifically targeted immediate identification and isolation of a patient at presentation, rapid triage, and timely (within 60 minutes of arrival) antibiotic administration. This standard posed a particular challenge to ED clinicians faced with an unpredictable patient volume and competing demands. Despite ongoing efforts over years to meet this standard, audits revealed a steady lengthening of time to antibiotic administration. A 1-year retrospective chart analysis of children who received antibiotics for fever and known neutropenia confirmed that $>50\%$ exceeded 60 minutes from time of initial arrival to antibiotic administration. Additionally, delivery time was highly variable ranging from 20 minutes to 3 hours. Due to the high risk for morbidity and mortality in this population, we considered improvement in this area a high priority.

### METHODS

#### Setting

Children’s Hospital Boston is a 390-bed pediatric academic institution and is a major cancer referral center. The ED is a level 1 American College of Surgeons certified pediatric trauma center with an annual volume of 60,000 visits and an admission rate of $\sim 20\%$. Approximately 25% of the patients are deemed high acuity by the emergency severity index.

Dana-Farber/Children's Hospital Cancer Center follows $\sim 2400$ patients. There are 1000 patients on active treatment. Per shift, there is a range of 2 to 8 ED attending physicians/fellows and 3 to 6 residents, 1 charge nurse, 1 to 3 triage nurses, and up to 14 registered nurses. There is at least 1 hematology/oncology fellow on call 24 hours a day.

### Improvement Team

A multidisciplinary team was formed consisting of an ED quality nurse leader and ED nursing and doctors along with staff nurses. Ad hoc members of the team included the ED pharmacist, ED administrator, security director, and oncology clinicians. Support was also provided by hospital quality improvement experts. The project was considered a quality improvement project and therefore did not require informed consent from individual patients/families.

#### Planning the Intervention

We developed a process map, studied it, and identified the key drivers necessary to decrease the time to antibiotic delivery (Fig 1). The identification of key drivers was facilitated through a brainstorming session of ED physicians, nurses, and a pharmacist (Fig 2). We reviewed examples of patients receiving timely antibiotics. We agreed that a target of 60 minutes to antibiotic delivery as stipulated in the CPG was optimal and should be applied to 100% of the patients. We recognized that the goal of 100% would be difficult to achieve; however, given the potential consequences of delay, we would strive to meet this goal for all patients. In addition, to reflect real-world practice, we elected to include a second group of patients who presented possibly but not definitely neutropenic. For this group, we set a target of 90 minutes to receipt of antibiotics to account for additional laboratory turnaround time for ANC. The guideline stipulates cefazidime as the antibiotic of choice for patients with neutropenia and longer-acting ceftriaxone for patients without neutropenia. We dichotomized patients into these 2 groups to optimize antibiotic choice for the patient.

The process map and key drivers revealed several important findings. First, we evaluated our system of patient identification and triage. Potentially neutropenic oncology patients were immediately identified and placed in protective isolation upon initial contact at triage by using a Fast Pass Alert system. The Fast Pass is a bright orange placard and was disseminated to families by the inpatient nurses on discharge after initiation of chemotherapy. It was designed to provide facility security personnel and triage nurses with a visual alert upon arrival and also contained important information regarding the appropriate sized needle required to access the patient’s central venous device. Although the Fast Pass was not new, we found that over time, its use had become inconsistent. Re-education of patients, families, and parking attendants was needed to ensure sustainability. Several communication issues were identified. First, prearrival information regarding likely neutropenia status was missing. A need to improve the transfer of vital information between the oncology team and the ED team was crucial. Collaborative meetings with oncology team leaders resulted in the re-education of oncology fellows to provide prearrival direction for the ED staff. Additionally, outreach to the communication center staff who record
telephone “expect calls” from referring physicians led to the development of a template that prompted inclusion of predicted ANC either from recent ANC result or chemotherapy. This template was available to the ED physician on the electronic tracking board. Patients whose ANC could not be predicted from the template were classified as potentially neutropenic, and ED providers would have to wait for blood testing results.

Furthermore, root cause analysis (RCA) revealed that although febrile oncology patients with neutropenia were reliably triaged by the ED nurse and expedited to the treatment area, the physician was not consistently notified. This caused significant delays in the initiation of antibiotics. The team focused on enhancing communication between the charge nurse, who was in direct contact with the triage nurse, and the treating physician.

Ongoing RCA helped elucidate that a change to the electronic medical record made access to the CPG more difficult for clinicians. The guideline was not perceived as readily available because it was no longer on a paper form. Therefore,

FIGURE 1
Process map for oncology patients with fever and neutropenia. CBC, complete blood cell; F&N, fever and neutropenia.

Expect line* = asks for:
- Last chemo
- Last laboratory results (CBC count and ANC)
- What antibiotics to give
The team prioritized education for clinicians regarding electronic guideline access. Our next intervention focused on optimizing Port-a-Cath access, which sometimes accounted for prolonged delays. When a new safety needle was introduced, some ED nurses began to experience technical difficulties and were not confident in their access abilities. Parents also shared concerns that multiple access attempts put their child at additional risk for contamination. Some expressed a preference for the inpatient oncology nurse to perform this procedure causing delays of 1 hour or more. A Port-a-Cath competency and skill-based re-education of all ED nurses was combined with an infection reduction initiative. In addition, parents occasionally forgot to apply topical anesthetic cream before arrival. Oncology nurse leaders were asked to reinforce parental application of topical anesthetic cream before an ED encounter.

Lastly, we collaborated with ED pharmacy leaders to create a process that would prioritize antibiotic preparation through monitoring of the electronic patient tracking system. They also used unit dosing to optimize efficiency. In some cases, delays occurred when the oncologist requested a medication not conventionally stocked in the ED pharmacy. Pharmacists were able to assist in access and rapid turnaround of the appropriate antimicrobial.

**Planning the Study of the Intervention**

The ED quality committee ensured leadership support and commitment for this improvement initiative. Project timelines were defined and accountability established. A team of process and subject matter experts was identified as champions for the change and was tasked with providing education to all personnel. A robust fever and neutropenia campaign was launched at a physician/nurse collaborative meeting in December 2008 where core knowledge and standards were communicated. A group brainstorming session followed where clinicians were asked to identify possible improvements. Key drivers were identified with the corresponding action plan. Nurses and physicians were asked to be the implementation arm of this initiative and operationalize these solutions at the bedside. Champions also ensured strategies were aligned with operations and deployed at all levels.

The Model for Improvement with its associated Plan-Do-Study-Act cycle was employed to test changes in iterative cycles. An automated patient identification report was created, and data were collected monthly on all eligible patients utilizing the electronic medical record. A case by case RCA was performed on patients who did not meet target goals. Real time coaching and feedback were provided by champions and positive efforts were recognized and celebrated. Results of every cycle were reviewed to evaluate the impact of strategies and determine the need for modifications. Clinicians were informed of progress monthly via e-mail and visual postings on the unit. Formal initiative updates with graphic data display were presented quarterly at a collaborative physician/
nurse forum and new strategies for success were shared.

Methods of Evaluation
The population of interest consisted of all oncology patients who presented to the ED with fever within the last 24 hours and had or possibly had an ANC of $<500$. The guideline defines fever as an axillary temperature of $\geq 38.3^\circ C$ (101°F) once, or $\geq 38.0^\circ C$ (100.4°F) for more than 2 hours in a 24-hour period. Patients who received antibiotics within 24 hours before arrival in the ED, such as those seen at an outside location before the ED visit, were excluded.

We sought to evaluate whether time to antibiotics improved from the pre-intervention period to the post-intervention period. The primary outcome was the proportion of patients with known neutropenia who received antibiotics within 60 minutes of arrival. A second group included those with possible but unconfirmed neutropenia who received antibiotics within 90 minutes of arrival with a target goal of 100%. Retrospective chart reviews were conducted monthly by using an audit tool designed to track delays identified as a “special cause” applying run chart rules were then subjected to RCA, and improvement strategies were employed to address these causes.

For balancing measures during the improvement period, we chose to follow the timeliness of first $\beta$-agonist treatment of patients with asthma and the left without being seen (LWBS) rate. Summary statistics were calculated by using mean for continuous variables and percentage for categorical variables. $\chi^2$ statistic was used for comparisons of demographics.

Analysis
We used statistical process control to monitor the process and to evaluate the impact of the intervention. Monthly averages of time to treatment and percent of patients who met target were plotted on run charts. These provided insight on high level variation in the process and were used to identify shifts or trends in the process before and after intervention. Control charts were used to plot time to treatment of consecutive patients and provided a ground level or patient to patient understanding of variation in time to treatment. The pre-intervention interval was October 2007 to December 2008, and the postintervention time was January 2009 to December 2010. During the preintervention period, prearrival information did not include the patients’ actual or predicted neutropenic status; therefore, the preintervention phase includes both groups. The mean time to antibiotics was calculated for the patients seen during each month and was plotted over time. We included a second analysis as above for patients in whom the neutropenic status was unknown on arrival, the possibly neutropenic group. We followed admitted patients prospectively for morbidity or mortality to determine if our intervention led to change in outcomes pre- and post-intervention.

RESULTS
The patients in the preintervention and postintervention period were similar in age, gender, race, oncologic diagnosis, and check-in time of day (Table 1). We were able to improve the mean time to antibiotics for patients with neutropenia from 99 minutes to 49 minutes and for those with possible neutropenia from 90 minutes to 81 minutes (Fig 3 A and B). Of the patients with possible neutropenia, 60% were ultimately found to be neutropenic. See Fig 3C for run chart of all patients combined. Although we did not meet the target of 100% of patients receiving antibiotics within the targeted time, we were able to improve the proportion who met the target from 50% to 88.5% (Fig 3D). Figure 4 shows an individual control chart of 25 consecutive patients. In the cases that did not meet the target, RCA elucidated delay or difficulty in accessing the Port-a-Cath in 9 patients. Most were due to special requests by parents regarding access. Four patients did not meet the target because of a delay in the physician placing an order for antibiotic.

We evaluated the outcomes of the patients by monitoring the rate of transfer to the ICU within 24 hours of admission as well as the mortality rate within 7 days of admission. There were no deaths and no unplanned transfers

<table>
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<tr>
<th>TABLE 1 Demographic Characteristics of Patients With Fever and Neutropenia in the Pre- and Postimplementation Phases</th>
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<td>Patient Characteristics</td>
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<td>Oncologic diagnosis, $n$ (%)</td>
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<td>Hematology malignancy</td>
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<td>Mean age, $n$ (range)</td>
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<td>Check-in time, $n$ (%)</td>
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<td>8:01 AM–4 PM</td>
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<td>4:01 PM–12 AM</td>
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FIGURE 3
A. Time from arrival to antibiotics for patients with fever and neutropenia. B. Time from arrival to antibiotics for patients with fever and possible neutropenia. C. Time from arrival to antibiotics for patients with fever and neutropenia, and possible neutropenia. D. Percentage of all patients who met targets.
from ward to the ICU within 24 hours of admission in both the preimplementation and postimplementation phase.

The balancing measure monitoring timeliness of delivery of first β-agonist treatment and percent meeting the time target for patients with asthma revealed no change during the quality improvement initiative. However, the LWBS rate dropped from 0.8% in the preintervention to ~0.4% in the post-implementation period.

**DISCUSSION**

By using the model for improvement,5 we were able to decrease the mean time to antibiotics by 50 minutes for patients with fever and neutropenia in a pediatric ED and improved those meeting the target to over 88%. The change was smaller for patients with possible neutropenia because we were already close to the target preintervention. However, we were able to decrease variability in time to antibiotics in this group.

The Infectious Disease Society of America has recommended that antibiotic therapy be administered promptly to neutropenic patients at the onset of fever,1 but no specific time window has been recommended. Timely antibiotic therapy has been a challenge for many institutions. In 1 improvement effort, improving the availability of antibiotics (placed on an emergency cart in the ICU) was the intervention that led to more timely antibiotic delivery, improving the median time to antibiotics from 164 to 55 minutes, but only 52% received antibiotics within 1 hour.6 There was no specific education or protocol introduced to the care team. Baltic et al7 studied the time to antibiotics in adult neutropenic patients on an inpatient unit. They assembled a multidisciplinary team to define areas for improvement. The bulk of the improvement effort, however, was in the building of a care algorithm and an associated packet of forms to facilitate care. Our challenge was to take the existing algorithm and successfully improve operationalization primarily by improving communication among the numerous stakeholders.
Variation in care processes can lead to confusion and error, especially in a busy and sometimes chaotic ED setting. Standardization requires stakeholder engagement and consensus. We believe the most important lesson from this effort was the affirmation that awareness, agreement, adoption, and adherence by the entire multidisciplinary team were essential to success. This particular project was challenging in that it required engagement of a wide variety of stakeholders. Despite this, we were able to unify all toward a common goal. The compelling imperative to provide timely treatment of a sick child with cancer was central to the ability to engage the team. This and the unified goal were fundamental to success.

Our primary key drivers were related to communication both within and outside of the ED. Dedicated meetings with senior ED and oncology physicians and nurses led to engagement and reinforcement of the process. The oncology team was highly invested in timely care for their patients and was already providing the ED team with prearrival information, so augmentation of the prearrival notification with expected ANC was an easy addition. Family activation is a powerful intervention and has shown to be effective in preventing inpatient cardiopulmonary arrest. The oncology team aligned with and activated families. By building on the families’ trust, they were able to support the ED process. This included informing families of the importance of contacting the oncology team when fever was apparent, applying EMLA at home, and allowing rapid catheter access. They were also able to enlist confidence in the ED nurses’ capabilities in accessing the catheters. Additional meetings with pharmacy and parking/security also assisted in alignment of all non-ED personnel involved.

The ED team was engaged by a joint physician/nurse session and separate nurse and physician educational and brainstorming forums to develop and then educate about the modified care process. Nurses can be particularly challenging to engage because many nurses work part-time or rotate shifts. The ED nurses therefore have developed a robust one-to-one education “tree” whereby each leadership nurse trains a small group that then is responsible for training other nurses individually until all have had one-to-one training. This has been a highly effective method for informing and engaging nurses in many ED initiatives. Communication with the ED-based pharmacists to stock and prioritize antibiotic preparation was also key.

Another element of success was engagement of senior nursing and physician leaders and opinion leaders in the ED. The division chief granted valuable conference time to discuss the effort while promoting a normative culture of quality. Well-respected clinical faculty actively embraced the initiative reinforcing and modeling compliance during ED shifts. Nursing leadership repeatedly championed the effort in charge nurse meetings, and individual charge nurses brought this awareness to the bedside.

General and individual feedback to all members of the team was helpful in reinforcing the process and keeping the team focused on the shared goals. Monthly performance reports were shared by e-mail and posters. This is in keeping with various studies that have revealed that timely, individualized feedback is most associated with and fundamental to improvement.

There were a few additional challenges in this effort. Despite working closely with families both before a febrile episode and within the ED at the time of the episode, there remained barriers to success. On several occasions, the parent insisted on placement of topical analgesia in the ED delaying antibiotics. Other parents continued to refuse access of the indwelling device by unfamiliar ED nurses. In the future, we could consider the use of a more rapid local anesthetic such as ethyl chloride. We continue to work with families and the oncology team to optimize timeliness.

Although we chose 2 balancing measures to control for potential deterioration in timeliness of care for other patients, it is possible that other clinical processes were delayed by this initiative. We did, however, choose a companion timeliness measure (first asthma treatment) that depended upon triage nurse action within the first 30 minutes of arrival for 1 of the most common conditions treated in our ED. We did not see deterioration in any standard ED throughput measures nor LWBS rates. No additional staffing resources were required to support the intervention; however, we did not measure direct effect on bedside nurse’s team when a febrile neutropenic patient was placed in his/her nursing district. We also recognize that there is potential for staff to develop user fatigue. This underscores the importance of having a sustainable program with continuous feedback regarding the positive outcomes in children with cancer.

Furthermore, improvement in our setting might not be generalizable in other ED settings. We were able to capitalize on various contextual factors and these may have contributed to the success of our intervention.

CONCLUSIONS

We developed and instituted a formal quality improvement initiative to reduce the time to antibiotics for febrile neutropenic patients. By applying quality improvement methodology specifically around the challenge of high level communication with and awareness by the multidisciplinary team, we were able to successfully reduce the time to antibiotic administration.
REFERENCES


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