



Implementation of a Nursing Based Order Set: Improved Antibiotic Administration Times for Pediatric ED Patients with Therapy-Induced Neutropenia and Fever

Tana Lukes, BA, BSN-RN, CPN^a,
Katharine Schjodt, MSN, APRN-PCNS-BC, CPN, CPHON^{a,*}, Leeza Struwe, PhD, MSN, RN^{a,b}

^a Children's Hospital and Medical Center, Omaha, NE, United States of America

^b University of Nebraska Medical Center, Lincoln, NE, United States of America



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ABSTRACT

Purpose: For patients with chemotherapy-induced neutropenia and fever, delays in antibiotic administration are associated with poor outcomes, such as ICU admission and need for further interventions. The objective of this quality improvement project was to significantly reduce the time from initiation of triage to antibiotic administration for pediatric patients arriving to the emergency department with therapy-induced neutropenia and fever. **Methods:** An interdisciplinary team set an evidence-based goal for time to antibiotics (TTA) at 60-min. A six-month retrospective chart review of Emergency Department (ED) patients revealed a 128 min TTA mean when measured from the initiation of triage to antibiotic administration, which also reflected 0% of patients receiving antibiotics within the goal of 60 min. Members of the interdisciplinary team evaluated delays in patient care workflow and identified three primary interventions to decrease the TTA. These three evidenced-based interventions were implemented and evaluated using the Plan-Do-Check-Act (PDCA) quality improvement methodology.

Results: By the end of the implementation period mean TTA improved to 53 min and patients received antibiotics within 60 min (83% of the time).

Conclusion: The interventions focused on both provider and nursing workflow, however the implementation of an evidence-based practice nursing order set made the greatest impact on timeliness of antibiotic delivery time.

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Introduction

For a child with cancer, a fever is a critical situation which necessitates prompt initiation of antibiotics to reduce morbidity and mortality (Ahmed & Flynn, 2018; Fletcher et al., 2013; Salstrom et al., 2015). Intravenous antibiotic therapy increases the number of healthcare visits, and potentially delays cancer treatment. An absolute neutrophil count (ANC) is a predictor of a patient's risk of infection, with ANC <500 indicating a patient is neutropenic and at severe risk for infection (Volpe et al., 2012). Kumar et al. (2006) showed in adult septic patients with hypotension that survival decreased on average 7.6% for every hour delay of antimicrobial administration within the first 6 h of hypotension presentation. Current adult and pediatric sepsis guidelines identify the importance of early administration of antibiotics, marking 1 h after recognition of sepsis as a reasonable goal (Rhodes et al., 2017). Fletcher et al. (2013) were also able to show when febrile pediatric neutropenic patients had antibiotics administered in >60 min, there was an

association with an increase in adverse outcomes, such as intensive care admission and need for fluid resuscitation. Furthermore, an additional study also showed a significant decrease in ICU admission when antibiotics were administered in <60 min for febrile pediatric oncology patients (Salstrom et al., 2015).

Local problem

Following a delay in antibiotic delivery that resulted in an intensive care unit stay for one patient, an interdisciplinary team worked to put quality improvement measures in place to improve promptness of antibiotic administration. In this organization, the Emergency Department (ED) provides initial treatment for the majority of neutropenic patients presenting with a fever, thus the ED became the logical starting point for this quality improvement project. The Emergency Department is a verified Level II pediatric trauma center within a regional 149-bed free-standing, Midwestern pediatric hospital. Annual number of visits are approximately 34,000 and the ED has a maximum of nine nurses and five providers working at one time, with varying staffing numbers throughout the day. Patients treated at this facility travel from a five-

* Corresponding author.

E-mail address: kschjodt@childrensomaha.org (K. Schjodt).

Table 1
Emergency severity index scale.

1	Requires life-saving intervention.
2	High risk situation, confused/disoriented/lethargic, severe pain/distress, cannot wait.
3	Many resources needed, consider "danger zone vitals".
4	One resource needed.
5	No resources needed.

Obtained from Gilboy, Tanabe, Travers, & Rosenau, (2012) "Emergency Severity Index (ESI)".

state region. This ED utilizes the Emergency Severity Index (ESI) (Table 1) scale to assist staff in prioritizing patient care and is used for all patients seen in the ED. Prior to the project, febrile neutropenic patients were consistently triaged as ESI level 2, however no other nursing guidelines were in place (Gilboy, Tanabe, Travers, & Rosenau, 2011).

Specific aims

The specific aims of this quality improvement project were to reduce the time to antibiotics (TTA) in the identified population from a mean of 128 min to <60 min, and to increase the percent of these patients who received antibiotics within 60 min from 0% to at least 50%. A goal time of 60 min or less was chosen based on current guidelines in literature to reduce morbidity and mortality (Ahmed & Flynn, 2018; Fletcher et al., 2013; Rhodes et al., 2017; Salstrom et al., 2015). Eventually, the goal would be to expand the quality improvement project to inpatient and additional outpatient areas.

Literature review

While the recommendation of prompt delivery of antibiotics is commonly recognized in the literature, "prompt" is often not explicitly defined. More recently a definition of <60 min for sepsis intervention has been used (Fletcher et al., 2013; Kumar et al., 2006; Rhodes et al., 2017; Salstrom et al., 2015). Current literature has many articles reviewing different organizations' quality improvement projects, however the nature of the current literature available has yet to produce strong supported evidence for which quality improvement methods are most effective. Cohen et al. (2016) were able to reduce TTA in pediatric patients by implementing a protocol, which included parent education on timeliness of obtaining central line access, nursing staff education on central line access, antibiotic availability in the department and providers not waiting for lab results prior to ordering antibiotics. Benner et al. (2018) also utilized a clinical practice guideline for pediatric patients which included multiple interventions including administration of antibiotics before lab results, utilizing a pre-arrival order set, and allowing nursing to establish IV access prior to provider assessment. Vedi et al. (2015) were able to have success decreasing time to antibiotics in children by not waiting for final lab results. In 2015, Salstrom et al. published a quality improvement initiative for pediatric patients which utilized several PDCA cycles and showed clinically relevant results of decreasing need for intensive care stays and decreased mortality with TTA <60 min.

One approach to decreasing TTA is to make standard doses of antibiotics available on patient care units, allowing nursing to have timely access to medications rather than waiting for a pharmacy to prepare (Amado, Vilela, Quieroz, & Amaral, 2011; Corey & Snyder, 2008). An additional delay identified by another facility was related to a need to improve competency of the nursing staff on accessing central line devices (Vedi et al., 2015). One organization was also able to decrease TTA for pediatric oncology patients through improved discussion during rounds for the patient's plan of care should a fever develop (Green et al., 2016). Implementation of an advanced practice nurse driven pathway proved beneficial for one organization to reduce their time to antibiotics for children (Vanderway, Vincent, Walsh, & Obrecht, 2017). Another organization utilized quality improvement methods to improve communication and utilization of a clinical practice guideline to improve time to antibiotics in a pediatric ED (Volpe et al., 2012). Additionally,

electronic order sets have been used to insure ready access to the application of best practices, enhance patient safety and care effectiveness (Poppy et al., 2016; Solomon & Jurica, 2017). One organization was also able to reduce TTA with the application of a standardized approach to treatment of febrile pediatric oncology patients with implementation of an order set (Cash, Deloach, Graham, Shirm, & Mian, 2014). Review of the available literature revealed a variety of approaches to reducing TTA, the project outlined here is one way to accomplish this.

Methods

Project design

The interdisciplinary group conducted a quality improvement project during June 2015 – March 2016 to reduce TTA for febrile, neutropenic pediatric patients. The group included hematology/oncology (H/O) and ED physicians and nurse practitioners, ED clinical nurses, the H/O Clinical Nurse Specialist (CNS), a pharmacist, and members of the Information Technology (IT) department.

The initial project step was to determine a specific patient population included in the quality improvement project. The designated inclusion criteria involved pediatric patients who: were receiving chemotherapy or other immunosuppressive drugs including, but not limited to, high dose steroids, calcineurin inhibitor, or mTOR inhibitor; had received a bone marrow transplant in the previous 100 days; and had experienced known bone marrow failure syndrome, aplastic anemia, or neutropenia and arriving to the ED with report of a temperature measurement of 38.0C (regardless of thermometer type used at home). Of note, this institution has Acute Myelogenous Leukemia (AML) patients stay inpatient through their neutropenic period, and on this basis would be excluded from this project. The exclusion criteria were defined as: patients receiving antibiotics prior to arriving to the ED; and patients presenting with non-therapy induced transient neutropenia.

The team conducted a six-month retrospective chart review using electronic medical record (EMR) reports to evaluate average TTA from January to June 2015 to establish baseline data. These reports were generated on patients that fit the inclusion criteria and included time stamps of each step in the patient's care starting at ED triage initiation and ending with antibiotic administration. This review reflected care provided to a total of 39 patients and established that none of the patients received antibiotics within the 60-min goal time (leaving the unit with a 0% success rate).

EMR reports gathered the following data:

- Patient name and medical record number (MRN)
- Time of triage
- Time of orders
- Time of antibiotic initiation
- Time blood cultures were drawn
- Pharmacy dispense time

After analyzing this baseline data (Table 2, cohort 0), the team identified delays in receiving provider orders and initiation of antibiotics. Using an evidenced-based approach, the team created interventions focused on altering this time. The three primary interventions were

Table 2
Outcomes by cohort in minutes (standard deviation) with percent under 60 minutes.

Cohort	N	Triage to First Order	Triage to Antibiotic	Triage to Blood Draw	Order to Antibiotic	Percent TTA in 60 min
0	39	83 (63)	128 (55)	65 (35)	45 (22)	0%
1	24	35 (34)	85 (41)	64 (47)	48 (24)	17%
2	17	37 (37)	98 (43)	54 (32)	61 (35)	24%
3	12	16 (13)	53 (27)	34 (30)	36 (20)	83%
4	99	18 (23)	60 (30)	40 (29)	44 (25)	67%

chosen as a result of baseline data evaluation: 1) creation of an EMR provider order set, 2) practice change to administer a broad-spectrum antibiotic before receiving laboratory results, and 3) creation of a triage nurse order set. As each intervention was implemented, data was evaluated utilizing the Plan, Do, Check, Act (PDCA) model (Tague, 2004).

Interventions

The initial intervention (Table 3, cohort 1) was aimed at improving provider workflow. The first step in this process involved collaboration with the IT department to create an order set accessible in the EMR for ED providers. The goal with this initial intervention was to promote accessibility of evidence-based orders, decrease delay, and promote patient safety.

The second intervention (Table 3, cohort 2) was aimed at changing both provider and nursing workflow. Previous practice in the ED was to wait for CBC results obtained during the ED admission and then determine antibiotic choice based on patient's neutropenic status. While the ANC is an important lab value to gather, this organization found that waiting for the ANC result was contributing to a delay in antibiotic delivery. The new intervention provided an order set that established the administration of a broad-spectrum antibiotic prior to CBC results. Then, once the medical team received lab results, patients with an ANC < 500 would receive additional antibiotic therapy based upon their actual CBC results. The interdisciplinary group felt the delay in antibiotics that was seen with the previous practice was a bigger risk than administering an additional dose of antibiotic.

The third and final intervention (Table 3, cohort 3) was the creation of a triage nurse order set which required the triage of all pediatric patients meeting the inclusion criteria to see a provider within 10 min using an ESI scale score of 2 (Table 1) (Gilboy et al., 2011). Other interventions outlined in the same nursing order set include: initiating peripheral intravenous (PIV) access in the absence of established central venous access; collection of labs (CBC and two sets of blood cultures); and administration of a weight-based broad-spectrum antibiotic. The nursing order set designated two antibiotic choices: ceftriaxone if non-neutropenic (defined as an ANC >500 or neutropenic status unknown), or cefepime (for neutropenic patients defined as a documented ANC < 500 within the last 48 h). The order set also requires the nurse to verify antibiotic choice with the provider. The orders in the nursing order set follow recommendations from the "Guideline for the Management of Fever and Neutropenia in Children With Cancer and/or Undergoing Hematopoietic Stem-Cell Transplantation" (Lehrnbecher et al., 2012). Throughout the three interventions, provider and ED nursing education was ongoing, not only in regards to the quality improvement interventions, but also about care of the neutropenic patient. Data was then evaluated twice later in the year for three-month intervals to confirm sustainability (Table 3, cohort 4).

Human subject protection

In the planning phases, the team contacted the organization's Institutional Review Board (IRB), and it was determined that the project did not constitute as human subject research and approval through the IRB was not required.

Table 3
Cohort descriptions.

Cohort Number	Cohort Dates	Cohort description
0	1/2015–6/2015	Baseline data prior to interventions
1	7/27/15–9/21/15	Intervention 1 (provider order set)
2	9/21/15–12/10/15	Intervention 2 (workflow change with lab results)
3	1/20/16–3/2/16	Intervention 3 (triage nurse order set)
4	5/16–7/16 and 9/16–11/16	Follow-up data evaluating sustainment

Data collection

During the intervention implementation periods, data was collected using EMR reports collecting the mentioned information. Once reports were generated, the inpatient oncology Clinical Nurse Specialist was the consistent person dedicated to chart reviews to ensure inclusion criteria were met.

Data analysis

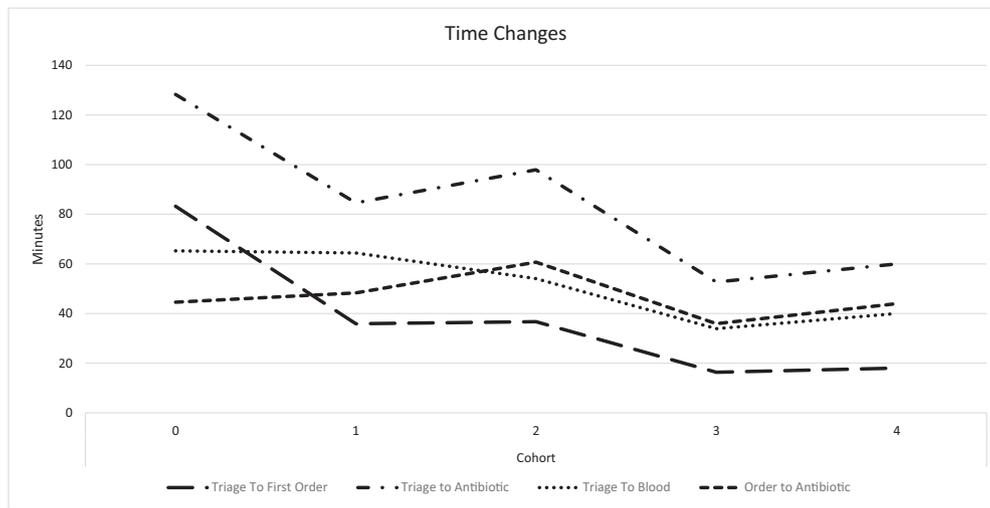
Data were entered into an Excel file, checked by a separate data entry method, and then converted to SPSS 25. Data were cleaned and the distributions were assessed. All of the outcome variables had significant outliers and due to the nature of the data (measuring time from 0 to 320 min), a normal distribution was not expected, and therefore a non-parametric test was utilized. An a priori alpha level of 0.05 was selected for all inferential testing. Variables were summarized using descriptive statistics (Table 2). A Kruskal-Wallis H test was conducted to assess for significant changes from baseline to each cohort for each outcome variable. The Kruskal-Wallis H test was chosen due to the non-normality of data distribution as this test can be used to determine if there are statistically significant differences between groups by using the median rank of the variable. When there are more than two groups a follow up test will need to be conducted to find significant differences at the group level while controlling for an increasing error rate when multiple tests are performed. For follow up testing, the Dunn's procedure was used along with a Bonferroni adjustment; together they adjusted the a priori alpha level to 0.01.

Results

A total of 101 patients were evaluated in cohorts in the time period of January of 2015 to November of 2016. Cohort groups of the pediatric patients were evaluated to measure the impact (time in minutes) of the initiation of each of the quality improvement interventions. The timing of these interventions and the measurement points following each intervention are reflected in Table 3, where each time period was given a cohort number. Table 2 provided data related to the measured changes in the outcomes variables. Descriptive analysis shows cohorts having a decreasing mean time and an increase in percentage of patients receiving antibiotics within 60 min of reaching triage, Table 2 and Graph 1.

Overall each cohort demonstrated consistent decreases in time for each outcome with the initiation of each new intervention. The primary aim of decreasing time of triage to antibiotic administration showed a significant difference between the baseline cohort 0 and three other cohorts, $\chi^2(4) = 75.1, p < .01$, with a cohort 0 median of 108 min, cohort 1 median of 77 min ($p = .039$), cohort 2 median of 91 min ($p = .891$), and cohort 3 median of 47 min ($p < .01$) with the sustainability cohort 4 having a median of 51 min ($p < .01$). Two of the other three outcomes were significant for change over time. The triage to first order and triage to blood draw also had significant decreases from baseline cohort to cohort 3 and from baseline to the follow-up cohort 4, all p -values were $p < .01$, Table 4. The last outcome, order to antibiotic, showed meaningful decreases, but was not statistically significant, $p = .07$, Table 4. In the sustainability cohort 4, there was a statistically significant increase in two of the four outcomes, triage to antibiotic and triage to blood draw, $p < .05$, Table 4.

An additional variable that was evaluated but is not included in the report because it was found to not contribute to delays in TTA, were pharmacy related time intervals. Pharmacy data were evaluated for total preparation time, including pharmacist dose verification and preparation, from July 30, 2015 – August 17, 2015 with an average of 10 min and again from September 22, 2015 to November 16, 2015 with an average of 13 min. In this setting the pharmacy is located next to the ED creating minimal delivery time for antibiotics.



Graph 1. Changes in mean time to first order, antibiotic order and administration, and blood culture draws by cohort.

Discussion

The strength of this project was collaboration through the interdisciplinary workgroup. It was through combined idea sharing and work of everyone involved that the outcome of improved TTA was produced. While the goals outlined by the project were met, additional work remains to improve patient outcomes. Through evaluation of project sustainment, while average TTA stayed within the goal time of 60 min, it began to slightly increase over time. This shows the importance of continued vigilance to ensure adoption of the quality improvement interventions. The creation of the triage nursing order set allowed nursing autonomy to be maximized. The improvement in TTA following implementation of the nursing order set is an example of how patient outcomes can improve with nursing autonomy. While each intervention contributed to decreases in TTA, the most significant decrease in time was seen following the nursing order set implementation.

Limitations

An identified limitation of this quality improvement project is the use of a convenience sample of pediatric patients. These findings may be unique to the participants in this specific setting, and suggests these results are not generalizable to other institutions. The data results were dependent on which patients walked through the ED door and their proximity to the hospital. Patients residing outside the metropolitan area would have already been treated at an outside ED and were not included in the data results. A potential factor in treatment time that was not gathered in the project data, includes patient mode of transportation to the ED, for example via private care or ambulance. However, regardless of transportation route, a febrile neutropenic patient would be triaged at the same level. In compiling results, an effort was not made to differentiate neutropenic vs. non-neutropenic patients with laboratory values; all patients meeting the inclusion criteria for the nursing triage order set were included. As with any workflow change,

there were some slow-adapters to the interventions. An identified limitation is that data on compliance of provider and nurse use of the order sets were not collected. Implementation of the nurse triage order set was also delayed for two months (December 10, 2015 to January 20, 2016) due to competing priorities that created a gap in the data. An additional variable that was not accounted for includes patient central line type, as this variable can impact total nurse care time. A final limitation includes the measured TTA beginning with “triage start”. These patients are flagged upon arrival to the ED, however there exists a small chance that the patient waited a certain number of minutes in the waiting room before arriving to triage.

Clinical implications

Through creation of an interdisciplinary group, collaboration across a care continuum was achieved to impact patient outcomes. Creation of the nurse triage order set allowed nursing autonomy to be maximized and staff nurses were able to make a significant impact in the care of this patient population. Through the three different interventions, various disciplines were able to have a part in improving patient care for this population.

Conclusion

Through this quality improvement project, this ED was able to increase collaboration between disciplines to impact patient care outcomes. TTA was decreased from an average of 128 min to <60 min utilizing three interventions. The interventions focused on provider and nursing workflow, improving nurse autonomy to effectively care for this patient population. Future projects could examine the process taking into account other variables, such as comparing patient line type to TTA, monitoring for intensive care admissions, and examining the process in inpatient settings and additional outpatient settings, such as an infusion center.

Conflict of interest

Authors declare no conflict of interest.

CRedit authorship contribution statement

Tana Lukes: Conceptualization, Project administration, Writing - original draft, Writing - review & editing. **Katharine Schjodt:** Conceptualization, Data curation, Writing - original draft, Writing - review & editing. **Leeza**

Table 4
Change in Outcomes by Cohort, Kruskal-Wallis H Test.

Outcome	Total N	Median Rank of Minutes by Cohort					df	χ2 value	p-value
		0	1	2	3	4			
Triage to first order	185	73	28	21	10	9	4	62.5	<0.01
Triage to antibiotic	189	108	77	91	47	51	4	75.1	<0.01
Triage to blood draw	179	57	49	45	25	34	4	38.9	<0.01
Order to antibiotic	191	44	46	53	34	38	4	8.7	0.07

Struwe: Formal analysis, Writing - original draft, Writing - review & editing.

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