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Original Article

Improving time to antibiotic administration in febrile neutropenia: A quality improvement initiative in a pediatric oncology inpatient unit

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ABSTRACT

Objective: Febrile neutropenia (FN) is a medical emergency requiring prompt initiation of empirical antibiotic therapy. We aimed to evaluate the impact of a structured, unit-based quality improvement intervention on time to antibiotic administration (TTA) in hospitalized pediatric oncology patients.

Materials and Methods: This single-center quality improvement study was conducted in a pediatric oncology inpatient unit. The intervention consisted of a structured educational program targeting healthcare professionals, including physicians and nurses. FN episodes were analyzed across pre-intervention, intervention, and post-intervention phases, and TTA was compared between these periods.

Results: A total of 73 FN episodes in 40 patients were included. Median TTA decreased from 38 minutes in the pre-intervention phase to 32 minutes during the intervention phase and to 18 minutes in the post-intervention phase ($p<0.001$). The proportion of patients receiving antibiotics within 60 minutes increased from 77% to 100% ($p=0.010$).

Conclusion: A structured, unit-based quality improvement intervention significantly reduced TTA in hospitalized pediatric oncology patients. These findings highlight the importance of system-level strategies in improving time-sensitive clinical processes in high-risk patient populations.

Keywords: Antibiotic, febrile neutropenia, quality improvement, oncology

Introduction

Febrile neutropenia (FN) is a life-threatening complication of cancer treatment requiring prompt medical intervention. It is defined as a single oral temperature ≥38.3°C or a sustained temperature ≥38.0°C for at least one hour in patients with an absolute neutrophil count (ANC) <500/mm³ or expected to decrease below this threshold within 48 hours (1).

FN remains a common clinical problem in pediatric oncology, occurring in up to 30–50% of patients undergoing chemotherapy, and is associated with significant morbidity and risk of bloodstream infections (2,3). Early initiation of empirical broad-spectrum antibiotics is the cornerstone of FN management. Current international guidelines strongly recommend administration of the first antibiotic dose within the first hour of fever detection (4-6). Despite these recommendations, delays in antibiotic delivery remain frequent in real-world clinical practice and are often related to workflow inefficiencies and communication gaps within healthcare teams.

The concept of quality improvement (QI) in oncology is based on identifying existing problems and implementing appropriate strategies to enhance patient outcomes and safety. The ASCO Quality Oncology Practice Initiative (QOPI) program aims to promote such QI efforts across outpatient oncology practices. The effectiveness of QI initiatives depends on addressing clinical, logistical, and administrative gaps. Ultimately, the goal of these interventions is to achieve sustainable improvement through collaboration, networking, and shared learning (7). Quality improvement interventions have emerged as effective strategies to optimize time-sensitive clinical processes in pediatric oncology settings. These interventions typically focus on system-level modifications, team training, and standardization of care

pathways to improve adherence to evidence-based practices. Several studies conducted in emergency departments have demonstrated that structured QI initiatives can significantly reduce time to antibiotic administration (TTA) and improve compliance with the one-hour target (8,9). However, data regarding inpatient settings, where workflow dynamics and team structures differ, remain limited.

In this study, we implemented a structured, team-based educational intervention as part of a unit-based quality improvement initiative in a pediatric oncology inpatient unit. The primary aim was to evaluate its impact on time to antibiotic administration (TTA) in febrile neutropenia episodes and to increase the proportion of patients receiving antibiotics within one hour of fever detection.

Materials and Methods

Study design and setting

This study was designed as a single-center, unit-based quality improvement (QI) initiative conducted in the Pediatric Hematology and Oncology inpatient unit of Istanbul University, between January 2023 and September 2023. The study was structured in accordance with the Standards for Quality Improvement Reporting Excellence (SQUIRE) guidelines (10).

Participants and study population

The study included pediatric oncology patients hospitalized for chemotherapy during the study period. A total of 40 patients were included, and 73 FN episodes were evaluated.

Intervention process

The intervention consisted of a structured, team-based educational program targeting healthcare professionals working in the inpatient unit, including residents, fellows, and clinical nurses.

The study was conducted in three sequential phases

Pre-intervention phase (3 months): FN episodes were recorded retrospectively based on routine clinical practice without additional training. No aspect of standard care was altered during this phase. During this phase, standard clinical practice was followed without any intervention, encompassing fever detection, staff notification, clinical assessment, antibiotic selection and prescription, and subsequent administration. Communication among healthcare staff and all steps involved in antibiotic administration were observed.

Intervention phase (3 months): A structured FN education program was implemented. Training sessions were delivered by a pediatric hematology and oncology specialist using standardized presentations. Each session lasted approximately one hour and was conducted weekly to ensure coverage of staff working in different shifts. Participants attended these sessions multiple times during the intervention period.

The training content included:

- recognition of febrile neutropenia
- risk assessment
- key components of physical examination
- selection and ordering of empirical antibiotics
- logistics of antibiotic delivery from the hospital pharmacy
- obtaining blood and other cultures prior to antibiotic administration
- confirmation of antibiotic administration
- communication and handover between shifts

Post-intervention phase (3 months): FN episodes were prospectively recorded following completion of the educational intervention.

Due to shift-based working conditions, not all team members were exposed to the intervention simultaneously. Repeated sessions were used to maximize coverage across the entire inpatient team.

Data collection and definitions

For each FN episode, the following data were recorded:

- time of fever onset
- time of temperature measurement
- time of notification of healthcare staff
- time of clinical assessment
- time of antibiotic prescription
- time of antibiotic administration
- total time to antibiotic administration (TTA)

Febrile neutropenia was defined as a temperature ≥38.3°C once or ≥38.0°C sustained for at least one hour, in the presence of neutropenia (absolute neutrophil count <500/mm^3 or expected decline within 48 hours). According to institutional protocols, empirical antibiotic therapy was initiated in all patients meeting FN criteria without waiting for culture results. The primary outcome of the study was TTA measured at the level of FN episodes. This study aimed to evaluate a unit-level clinical process indicator rather than individual healthcare worker performance.

Team performance was indirectly assessed through improvements in process-of-care indicators, particularly time to antibiotic administration (TTA), rather than through individual-level performance metrics.

Statistical analysis

Statistical analyses were performed using SPSS version 23.0 (IBM Corp., Armonk, NY, USA). Continuous variables were summarized using means and standard deviations or medians and interquartile ranges, as appropriate, while categorical variables were presented as frequencies and percentages. Comparisons between groups were conducted using Student's t-test or one-way analysis of variance (ANOVA) for continuous variables and the chi-square test for categorical variables. A two-sided p value < 0.05 was considered statistically significant. Because some patients contributed multiple FN episodes, comparisons across study phases were additionally performed using a linear mixed-effects model with a patient-level random intercept to account for within-patient clustering.

Results

A total of 73 febrile neutropenia (FN) episodes in 40 patients were included in the analysis. Of the patients, 17 (42.5%) were female. The distribution of underlying diagnoses was as follows: leukemia (n=15), neuroblastoma (n=6), lymphoma (n=5), brain tumor (n=4), hepatoblastoma (n=3), Ewing sarcoma (n=3), and

Table I: Clinical characteristics of participants

Characteristics	Study group
Total number of patients	40
Gender*	
Male	23 (57.5)
Female	17 (42.5)
Age†	7.2±5.3/6.0
Disease duration†	1.4±1.0/1.3
Age at diagnosis†	6.4±5.2/5.1
Disease Group*	
Leukemia	15 (37.5)
Neuroblastoma	6 (15)
Lymphoma	5 (12.5)
Brain tumor	4 (10)
Hepatoblastoma	3 (7.5)
Ewing Sarcoma	3 (7.5)
Others	4 (10)
Education status of parents*	
Primary/Secondary School	23 (57.5)
High School	7 (17.5)
University	10 (25)

**: n(%), †: mean±SD year/median*

Table II: Comparison of Time to antibiotic (TTA) dependent on quality improvement intervention

Values	Pre-Intervention	Post-Intervention	p
Total number of episodes	31	21	-
Time to antibiotic administration, min			
mean±SD**	47.3 ± 25.3	21.7 ± 9.4	<0.001*
95% CI of the mean	38.1–56.6	17.4–26.0	
median (IQR)	38 (32–52)	18 (16–23)	<0.001†
range	30–135	14–55	
antibiotic administered within 1 h, n (%)	24 (77.4)	21 (100.0)	0.033‡

**: Welch t test, †: Mann–Whitney U test, ‡: Fisher exact test, CI: confidence interval*

Table III: Effect estimates for the difference between the pre-intervention and post-intervention phases

Measure	Estimate (95% CI)	Test statistic	p
mean difference, min	−25.7 (−35.7 to −15.6)	t = 5.15, df = 41.0	<0.001
median difference, min*	−19.0 (−25.0 to −15.0)	U = 611	<0.001
relative reduction, %	−53.0 (−61.8 to −42.2)	-	-
Cohen d	−1.25 (−1.86 to −0.65)	-	-
rank-biserial correlation	−0.88	-	-

: Hodges–Lehmann estimator. Negative differences indicate shorter time to antibiotic administration. **CI: confidence interval, **df:** degrees of freedom.*

other malignancies (n=4). The mean age was 7.2±5.3 years (median, 6 years). The mean disease duration was 1.4±1.0 years (median, 1.3 years), and the mean age at diagnosis was 6.4±5.2 years (median, 5.1 years) (Table I).

Time to antibiotic administration

The mean time to antibiotic administration (TTA) was 47.3±25.2 minutes (median, 38.0 minutes) in the pre-intervention phase, 32.8±2.5 minutes (median, 32.0 minutes) during the intervention phase, and 21.6±9.4 minutes (median, 18.0 minutes) in the post-intervention phase. TTA decreased significantly from the pre-intervention phase to the post-intervention phase. (p<0.001) (Table II-III).

Table IV: Comparison of Time to Antibiotic (TTA) dependent on tumor type among all event

Characteristics	Leukemia	Lymphoma	Other Solid Tumors	p
Total number of episodes	24	13	36	-
Time to Antibiotic (TTA) min*	27.9±10.4 (30)	35.9±12.9 (37)	40.9±25.3 (32)	0.048

**: mean±SD (median)(One-way ANOVA), post hoc Tukey test showed significance between leukemia and other solid tumors (p=0.030).*

Table V: Comparison of Time to Antibiotic (TTA) within each tumor type group based on intervention

Characteristics	Pre-Intervention	Post-Intervention	p
Leukemia*	34.0±6.9 (30)	23.2±11.1 (20)	0.070
Lymphoma*	42.1±9.0 (40)	18.0±5.2 (16)	0.010
Other Solid Tm*	51.8±30.9 (38)	19.0±2.0 (18)	<0.001

**: mean±SD (median)(Student T Test)*

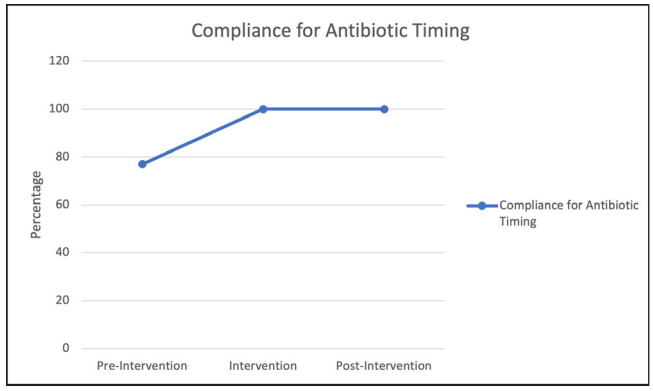

Figure 1: The change in the percentage of compliance for antibiotic timing (the percentage shows the rate of children receiving antibiotics in less than 60 minutes)

Percentage of patients receiving antibiotics within 60 minutes

The proportion of FN episodes in which antibiotics were administered within 60 minutes increased from 77% in the pre-intervention phase to 100% in post-intervention phase (p=0.010) (Figure 1).

Subgroup analysis by disease type

Across all FN episodes, the median TTA was 30 minutes among patients with leukemia, 32 minutes among patients with solid tumors, and 37 minutes among patients with lymphoma (Table IV). In disease-specific analyses, TTA decreased after the intervention across all diagnostic categories. This reduction did not reach statistical significance among patients with leukemia (p=0.070), but it

was significant among those with lymphoma (p=0.010) and solid tumors (p<0.001) (Table V).

Additional analyses

TTA did not differ significantly according to parental educational status (p=0.510). No FN-related mortality occurred during the study period. No patient contributed episodes to both the pre-intervention and the post-intervention phase, so the two groups are independent samples. Repeated episodes within each group nevertheless remain a source of clustering (52 episodes from 29 patients; intraclass correlation coefficient 0.77). A linear mixed model with a patient-level random intercept yielded a mean difference of –29.6 min (95% CI –45.8 to –13.5; p < 0.001), confirming the finding with a wider confidence interval.

Discussion

In this study, we demonstrated that a structured, unit-based educational intervention significantly reduced time to antibiotic administration (TTA) in hospitalized pediatric oncology patients with febrile neutropenia. The reduction in TTA was observed consistently across all study phases, with the most pronounced improvement in the post-intervention period.

Timely initiation of empirical antibiotic therapy remains a cornerstone of febrile neutropenia management. FN continues to be associated with substantial morbidity in pediatric oncology patients, with bloodstream infections representing the most common documented source of infection and reported mortality rates ranging from 0.4% to 3% (3,11,12). For this reason, international guidelines recommend administration of the first dose of antibiotics within one hour of fever detection (8).

Previous studies have shown that quality improvement interventions can effectively reduce TTA, particularly in emergency department settings. In one such study, implementation of a structured educational and process-based intervention reduced TTA from 64 minutes to 53 minutes and increased the percentage of patients receiving antibiotics within one hour from 59% to 84%, with further improvement after iterative cycles (13). Similarly, other studies have reported increased compliance with timely antibiotic administration following targeted interventions, with rates improving from 30% to 80% (14). In a comparable inpatient-focused intervention, the implementation of a structured protocol resulted in a reduction in mean TTA from 48 minutes to 39 minutes and achievement of full compliance within one hour (15).

Our findings are consistent with these studies and extend the existing literature by demonstrating that similar improvements can be achieved in inpatient settings. Unlike emergency departments, inpatient units involve different workflow dynamics, including shift-based care and multidisciplinary coordination. In this context, delays in antibiotic administration are often related to system-level factors such as communication gaps, unclear task allocation, and logistical barriers.

In the present study, the intervention primarily targeted these system-level processes. The observed improvement in TTA suggests that delays were largely attributable to workflow inefficiencies rather than clinical decision-making. Reinforcing team communication, clarifying responsibilities, and standardizing critical steps in patient management appeared to play a key role in improving timely antibiotic delivery.

Recent studies have questioned the strict association between TTA and clinical outcomes. Some investigations have reported no significant difference in mortality, intensive care unit admission, or length of hospital stay between patients receiving antibiotics within or beyond 60 minutes (16-18). These findings suggest that TTA alone may not be a direct surrogate for clinical outcomes. However, TTA remains an important quality-of-care indicator, reflecting the efficiency and responsiveness of healthcare systems in managing time-critical conditions. However, TTA remains an important quality-of-care indicator, reflecting the efficiency and responsiveness of healthcare systems in managing time-critical conditions (19-20).

Limitations

This study has several limitations. First, it was conducted in a single center with a relatively small sample size and short study duration. Microbiological data, including blood culture results, were not systematically analyzed in this study and therefore were not included. Second, although the intervention targeted healthcare professionals, outcomes were measured at the level of FN episodes, and individual healthcare worker performance was not assessed.

Despite these limitations, this study highlights the effectiveness of structured, team-based educational interventions as part of a quality improvement strategy in reducing delays in antibiotic administration in pediatric oncology inpatient settings.

Conclusion

This study demonstrates that a structured, unit-based educational intervention can significantly reduce time to antibiotic administration in hospitalized pediatric oncology patients with febrile neutropenia. The findings suggest that delays in antibiotic delivery are largely related to modifiable system-level factors and can be improved through targeted quality improvement strategies.

While the impact of TTA on clinical outcomes remains a subject of ongoing investigation, optimizing time-sensitive care processes represents an important component of high-quality clinical practice. Further studies are needed to evaluate the effect of such interventions on patient-centered outcomes, including morbidity and healthcare utilization.

Main points

- Febrile neutropenia is a time-critical clinical condition requiring prompt antibiotic administration in pediatric oncology patients
- Quality improvement strategies targeting system-level processes can effectively reduce delays in antibiotic delivery
- In this study, a structured educational intervention significantly decreased time to antibiotic administration (TTA)
- The percentage of patients receiving antibiotics within 60 minutes increased from 77% to 100% following the intervention

Ethics committee approval
This study was conducted in accordance with the Helsinki Declaration Principles. The study was approved by Istanbul University (06.01.2023, reference number: 2023/28).

Contribution of the authors
Study conception and design: YY, HGT; data collection: YY, CCE, EMAP, SS, GE, OK, PT, VK, GG ; analysis and interpretation of results: YY, HGT, DT; draft manuscript preparation: YY, HGT. All authors reviewed the results and approved the final version of the article.

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Conflict of interest
The authors declare that there is no conflict of interest.

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