Implementation of a Clinical Management Pathway to Shorten Time to Antibiotic Delivery in Febrile Patients With Sickle Cell Disease in a Pediatric Emergency Department

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Abstract

Background: Children with sickle cell disease are at increased risk for serious bacterial infections due to functional asplenia. When these children present for evaluation for fever, early administration of empiric antibiotics reduces morbidity and mortality. The American Academy of Pediatrics recommends that antibiotics be administered within 60 minutes of presentation to the hospital. Our primary objective was to shorten the time to delivery of the first dose of antibiotics for patients with sickle cell disease and fever in our pediatric emergency department by creating and implementing a clinical management pathway.

Methods: We developed a clinical management pathway for treatment of febrile children with sickle cell disease. Data for pre- and post-intervention cohorts were obtained using a retrospective chart review of pediatric emergency room encounters where a history of both fever and sickle cell disease were documented. The primary outcome measured was time to first dose of antibiotics, which was compared between pre- and post-intervention using a two-sample t-test. Secondary outcomes included the percentage of patients who received appropriate laboratory work-up and appropriate antibiotics.

Results: After implementation of the pathway, time to first dose of antibiotics decreased significantly from 2.22 hours (SD = 1.36; n = 46 visits) to 1.56 hours (SD = 1.13; n = 69 visits) (P = .006). The percentage of patients who received appropriate laboratory work-up and appropriate antibiotics also demonstrated a statistically significant improvement following intervention.

Conclusions: Implementing a standardized, evidence-based clinical management pathway for administering antibiotics quickly to febrile children with sickle cell disease can be an effective strategy for improving care in the pediatric emergency department.
non-vaccine preventable strains of pneumococcus still cause invasive disease. More recently, the 13-valent pneumococcal protein-conjugate vaccine (PCV13) was introduced. Its impact on the incidence of serious bacterial infection in patients with SCD, however, remains to be seen. Therefore, despite improvements in vaccine prevention, this patient population remains vulnerable to serious morbidity and mortality resulting from serious bacterial infection.

Fever can be the first sign of serious illness in the patient with SCD and should be treated as a medical emergency, triggering aggressive laboratory evaluation as well as empiric antibiotic therapy. Typical antibiotic selection for treating the stable SCD patient with fever is a third-generation cephalosporin such as ceftriaxone, thanks to its effective coverage of most strains of pneumococcus and its broad spectrum of activity. In the unstable patient, high doses of ceftriaxone are used in conjunction with an anti-staphylococcal antibiotic such as vancomycin. This combination therapy should be considered strongly in communities where resistant pneumococcal bacteria strains are prevalent.

There is significant interest in identifying SCD patients with fever who are at the greatest risk of invasive bacterial infections to help guide disposition. Unfortunately, not a single set of universally accepted risk criteria exists, as most studies were performed in the pre-PCV7 vaccine era.

In addition to any risk criteria used, it is important to obtain patient care information and advice from the patient’s primary pediatric hematologist to help guide disposition and discharge planning. The hematologist is likely aware of the patient’s baseline hematologic values, past medical history, and current risk status.

The American Academy of Pediatrics (AAP) has published best practice recommendations for children with SCD, including recommendations for managing these patients in the setting of fever. The AAP recommends administering parenteral, broad-spectrum antibiotics to patients within 60 minutes of triage. Additionally, the minimum recommended laboratory evaluation should include a complete blood count (CBC), reticulocyte count, and blood culture. These recommendations are consistent with many published guidelines. Specifically, the 60-minute threshold aligns with the American College of Critical Care Medicine recommendations for managing pediatric and neonatal septic shock.

Febrile patients with SCD frequently present to the emergency department (ED) for evaluation. As a result, demand is increasing for rapid patient transit through the ED, as prolonged length of stay has been linked to reduced quality of care and a rise in adverse events.

It is also critical that the ED provider be allowed sufficient time to consider situations necessitating a greater degree of complex clinical decision making while still providing efficient, high-quality care to a high volume of patients. One way to help facilitate this goal is to implement clinical management pathways for commonly occurring patient complaints where best practice guidelines exist. The goal of these pathways is not to supplant clinical decision making, but rather to provide a framework that increases efficiency and quality of care through compliance with best practice guidelines.

Preliminary analyses demonstrated that the recommended 60-minute threshold for administering antibiotics was not met in the majority of encounters in our pediatric ED. Therefore, as a quality improvement measure to shorten the average delivery time of the first dose of antibiotics to less than 60 minutes as recommended by the AAP, we created and implemented a clinical management pathway for patients with SCD and fever. Secondary aims included improving antibiotic selection and ensuring that patients receive the minimum recommended laboratory evaluation.

Methods

A clinical management pathway for patients presenting to our pediatric ED with both SCD and fever was developed in collaboration with a pediatric ED physician and a pediatric hematologist/oncologist. Recommendations for laboratory work-up, antibiotic choice, and risk stratification criteria were determined by evidence-based literature review and AAP best practice recommendations. Once created and approved by both departments, the pathway was presented to all ED physicians and nursing staff 1 week before implementation (April 1, 2014) (Fig. 1). The pathway was again presented approximately halfway through the intervention period at a department-wide morbidity and mortality conference that highlighted a case of pneumococcal septic shock in a young child with SCD. The pathway was also posted prominently at physician and nursing staff work stations inside the ED.

A retrospective chart review was completed for 1 year before intervention (March 2013–March 2014) and 1 year after intervention (March 2014–March 2015).
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2014) and after intervention (April 2014–April 2015). Chart review was conducted by a single physician reviewer (J.L.). Pre-intervention reviews were completed in 6-month intervals. Post-intervention reviews were completed in 3-month intervals.

Inclusion criteria for a patient encounter were 1) a documented International Statistical Classification of Disease-9 code for SCD in any ED visit, 2) patient age 2 months to 18 years, and 3) a documented objective or subjective history of fever. Although a numerical threshold for fever was used in the pathway, none was used in the chart review since this threshold was not reliably documented in the patient’s medical record. For inclusion in the study, a history of fever needed only to be noted in the medical record by physician or nursing triage documentation. All patient encounters occurring within the specified date ranges, and meeting all inclusion criteria, were included in the study.

Data collection included triage time, antibiotic administration time, name of antibiotic administered, laboratory studies obtained, blood culture result (if obtained), and length of stay (if applicable).

Triage time was considered to be time zero. End time was the time of antibiotic administration as documented by nursing staff. Antibiotic selection was considered appropriate when it included 1 of those recommended in the management pathway.

Figure 1
Clinical management pathway for febrile patients with sickle cell disease who present to the pediatric ED.

<table>
<thead>
<tr>
<th>Clinical Low-Risk Criteria</th>
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<tbody>
<tr>
<td>&gt;12 months • Well-appearing • No concerns for VOC, sequestration, ACS • Tolerating PO • No new hypoxia • Oxygen saturation ≥92% if unknown baseline • Room air saturation &lt;3% below baseline</td>
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<tr>
<th>Sickle Cell Disease w/Fever</th>
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<tr>
<td>2 months to 18 years old</td>
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<tr>
<th>Current Temp OR History of Temp</th>
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<tr>
<td>≥101.5 F</td>
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<table>
<thead>
<tr>
<th>Empiric Antibiotics</th>
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<tbody>
<tr>
<td>Within 60 minutes of triage*</td>
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<table>
<thead>
<tr>
<th>Rocephin</th>
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<tbody>
<tr>
<td>50-75 mg/kg/dose</td>
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<td>Max dose 2 grams</td>
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<tr>
<th>Clindamycin</th>
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<tbody>
<tr>
<td>10-15 mg/kg/dose</td>
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<tr>
<td>Hx of cephalosporin allergy (max 1.6 grams)**</td>
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<tr>
<th>Vancomycin &amp; Rocephin</th>
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<tr>
<td>15 mg/kg/dose</td>
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<td>75-100 mg/kg/dose</td>
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<tr>
<td>If unstable/septic</td>
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<tr>
<th>Laboratory</th>
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<tbody>
<tr>
<td>All Patients: CBC with diff, retic, BMP, blood culture</td>
</tr>
<tr>
<td>Case Dependent: Lumbar puncture w/routine CSF studies, CXR, CRP, procalcitonin</td>
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<th>Social/PMHx Low-Risk Criteria</th>
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<tbody>
<tr>
<td>No hx of Rocephin in last 8 weeks, bacteremia, sepsis, sequestration, multiple visits for same febrile illness • No hx of PCN noncompliance, delayed immunizations • Likelihood of good follow-up (reliable phone/car, no hx of missed appts, not in shelter)</td>
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</tbody>
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<table>
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<tr>
<th>All Patients</th>
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<tbody>
<tr>
<td>Contact hematologist on call to discuss disposition/follow-up</td>
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</tbody>
</table>

* Abx should not be delayed for lab studies.
** PCN allergies are not a contraindication to Rocephin.
or when an equivalent drug was given based on its spectrum of activity, patient allergy, or a documented contraindication.

An independent two-sample t-test assuming similar variances for individuals presenting before and after intervention was conducted to compare the average time to first antibiotic for the pre- and post-intervention cohorts. An independent two-sample test of proportions (Z) was conducted for each percentage that received ceftriaxone or another appropriate antibiotic, had a blood culture obtained, had a CBC obtained, and had a reticulocyte count obtained. All analyses were conducted in SAS (version 9.3, SAS Institute). A statistical threshold of .05 was used for all tests as a measure of statistical significance.

Results

A total of 121 unique patient encounters were reviewed and included in the data analysis.

The pre-intervention cohort included 52 patients; the post-intervention cohort included 69 unique patient encounters. All encounters occurred in the same pediatric ED. When determining mean time to first dose of antibiotics in the pre-intervention cohort, 6 patients were not included because they did not receive any antibiotics in the ED. However, these excluded patient encounters were considered in other analyses because the patients received a laboratory work-up.

Overall, mean time to antibiotic administration was significantly shorter in the post-implementation cohort (pre-implementation: 2.2 hours vs. post-implementation: 1.56 hours; \( P = .006 \)) (Table 1) (Fig. 2). Moreover, the proportion of patients who received antibiotics within 60 minutes of triage increased significantly following pathway implementation (17.4% vs. 37.9%; \( P = .010 \)) (Table 2). The proportion of patients who received antibiotics between 1 and 2 hours of triage also increased post-implementation. This increase, however, was not statistically significant (30.4% vs. 39.1%; \( P = .170 \)) (Table 2). The proportion of patients who received antibiotics more than 2 hours from triage was significantly lower following pathway implementation (52.2% vs. 23.2%; \( P < .001 \)) (Table 2).

A significantly higher proportion of patients received appropriate antibiotics following pathway implementation (pre-intervention: 86.5% vs. post-implementation: 98.6%; \( P = .004 \)) (Table 3). The rate of recommended laboratory work-up performed was also significantly improved: blood

<table>
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<tr>
<th>Table 1</th>
<th>Average time (hours) to first dose of antibiotics pre- versus post-intervention.</th>
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<tbody>
<tr>
<td></td>
<td>Pre-Intervention Cohort</td>
</tr>
<tr>
<td>N</td>
<td>46</td>
</tr>
<tr>
<td>Time to first dose (hours), mean ±SD</td>
<td>2.22 (±1.36)</td>
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<th>Table 2</th>
<th>Breakdown by time for first dose of antibiotics pre- versus post-intervention.</th>
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<tr>
<td></td>
<td>Pre-Intervention Cohort</td>
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<tr>
<td>N</td>
<td>52</td>
</tr>
<tr>
<td>Time to first dose, no. (%)</td>
<td></td>
</tr>
<tr>
<td>≤60 mins</td>
<td>9 (17.3)</td>
</tr>
<tr>
<td>&gt; 60 mins and &lt;120 mins</td>
<td>16 (30.8)</td>
</tr>
<tr>
<td>≥120 mins</td>
<td>27 (51.9)</td>
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SD, standard deviation
culture (86.5% vs. 97.1%; \( P = .0142 \)), CBC (90.4% vs. 98.6%; \( P = .020 \)), reticulocyte count (55.8% vs. 81.2%; \( P = .001 \)), and basic metabolic panel (BMP) or complete metabolic panel (CMP) (65.4% vs. 87.0%; \( P = .002 \)) (Table 3).

From the 112 blood cultures reviewed in the 2-year study period, 5 had positive results (4.4%). Of these 5 cultures, 3 were classified as contaminants and 2 as clinically significant. One of the positive cultures was Streptococcus pneumoniae with the patient developing septic shock (0.89% of all collected blood cultures). Approximately 41.3% of all study patients were admitted to the hospital. Mean length of stay was 3.7 days.

Discussion

These data showed implementation of a clinical management pathway in our pediatric ED to have a significant impact on the timeliness and quality of care provided to pediatric patients with SCD and fever. While the overall mean time to first dose of antibiotics was still higher than 60 minutes post-pathway implementation, we did experience a significant increase in the proportion of patients treated within 60 minutes (\( P = .010 \)) and a significant decrease in patients waiting more than 2 hours (\( P < .001 \)).

Appropriate antibiotics were administered in 98.6% of encounters in the post-intervention group. This figure was significantly higher than the pre-intervention group, demonstrating the priority placed on timely administration of appropriate antibiotics in the clinical management pathway (\( P = .004 \)). Significant improvements were also seen in the proportion of patients who received the recommended laboratory tests outlined in the pathway, including blood cultures, CBC, reticulocyte count, and BMP or CMP.

The incidence of bacteremia in febrile patients with SCD varies in the literature, with reports ranging from 0.8% to 4.0%. The specific incidence of pneumococcal bacteremia in one study was 0.4%. Our rate of bacteremia was consistent with the findings reported in the literature. The blood culture positivity rate was 4.4%, including pathogenic and suspected skin contaminant bacteria. The incidence of true pathogenic bacteremia, however, was 1.8%. We had 1 case of pneumococcal bacteremia, correlating with a 0.9% incidence rate.

Similar published quality improvement initiatives for pediatric patients with SCD and fever were not identified in our literature review. One study by Rutman et al reported on a clinical management pathway targeted toward increasing evidence-based care delivered to patients with asthma in a pediatric ED. Similar to our findings, they demonstrated statistically significant improvements in care following pathway implementation.

Two other studies sought to decrease the time to less than 60 minutes in providing antibiotics for neutropenic patients in the pediatric ED. Neutropenic patients represent a high-risk population, similar to those with SCD. Both studies yielded statistically significant decreases in the time to first dose of antibiotics and were able to achieve an average time of less than 60 minutes.

These studies’ findings, as well as ours, support implementation of a standardized treatment approach, such as a clinical pathway, for improving patient care within a pediatric ED. Given the success of these other studies, we are hopeful that our pathway will continue to yield further sustainable improvements.

The strength of our project centered on a multi-disciplinary approach to solve a substantial clinical problem and improve quality of care. Tremendous clinician and staff support existed for the project among both the Emergency Medicine and Hematology/Oncology units.

This study has all the inherent limitations associated with a single-center, retrospective study. Retrospective chart review studies are only as
strong as the documentation contained within the records reviewed. It is possible that important medical decision making was not documented. This fact would be especially important in cases where antibiotics were never administered to a patient.

**Future Directions**

Future directions for this project include the integration into our electronic medical record of a “Best Practice Advisory” with built-in “hard stops.” This innovation will require triage personnel to acknowledge the patient’s history of SCD and chief complaint of fever at the time of triage.

## References

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