The Use of Incentive Spirometry in Pediatric Patients With Sickle Cell Disease to Reduce the Incidence of Acute Chest Syndrome

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Introduction: To determine if incentive spirometry (IS) in pediatric patients admitted with sickle cell disease for nonrespiratory complaints will decrease acute chest syndrome (ACS).

Methods: This was an Institutional Review Board-approved before-after 2-year retrospective cohort study evaluating an evidence-based guideline (EBG) initiating mandatory IS in admitted pediatric sickle cell patients from a tertiary children's emergency center. Student t testing and χ^2 analysis were performed.

Results: There were 1551 patient visits. About 258 visits were enrolled in the pre-EBG year, and 230 in the EBG year. Between year characteristics were similar. The EBG year reported higher use of hydroxyurea ($P < 0.01$), analgesics ($P = 0.02$), and chest pain ($P = 0.03$). Sixty-seven patients (25.9%) in the pre-EBG year received transfusions versus 51 (22.5%) in the EBG year (NS). Twenty-five (9.6%) of the pre-EBG patients received blood for ACS versus 14 (6.1%) in the EBG group (absolute risk reduction: 3.5%, 95% confidence interval: −1-8.4%). Subgroup analysis revealed that patients who presented with back pain experienced a significant decrease in the development of ACS in the EBG year ($P = 0.04$, absolute risk reduction: 14%, 95% confidence interval: 1-28%, number needed to treat: 8).

Conclusion: Mandatory IS for sickle cell disease patients admitted without respiratory complaints reduces transfusions and ACS, particularly for those presenting with back pain.

Key Words: acute chest syndrome, sickle cell disease, emergency department, incentive spirometry

(*J Pediatr Hematol Oncol* 2011;33:415–420)

Sickle cell disease (SCD) is an inherited disorder of hemoglobin formation that can lead to injury to multiple organ systems. It is the most common single gene disorder in African-Americans,[1] affecting over 50,000 people living in the United States.[2] An estimated 9% of African-Americans have sickle cell trait with approximately 1 in 600 manifesting the disease.[3] The complications associated with SCD results in a decreased life-span in almost all forms of SCD. The frequency of illness and hospitalizations results in a burden on patients, their families, and the healthcare system.

Data gathered by the Healthcare Cost and Utilization Project showed that 25% of hospitalizations for SCD, 19,000 hospitalizations in 2004 alone, occurred in the pediatric age group. Of those hospitalizations, 27% were associated with pulmonary conditions.[4] The majority of SCD-related costs are attributable to the cost of hospitalization.[5] Thus, methods to reduce pulmonary complications while simultaneously reducing length of stay are desirable.

Acute chest syndrome (ACS) is a pulmonary complication that represents the most frequent cause of death in patients with SCD[6] and is the second leading cause of hospitalization in children with sickle cell disease.[6,7] A subgroup of patients develop ACS in the hospital at rates reported as high as 50%,[7] despite being admitted for other reasons such as fever. A limited number of studies have published attempts to reduce this complication. Bellet et al[8] previously reported that incentive spirometry (IS) reduced the incidence of ACS in 29 patients admitted with pain above the diaphragm. Hsu et al[9] showed that a positive expiratory pressure (PEP) device and IS were tolerated in patients with SCD. Despite the relative paucity of data on whether or not IS/PEP therapy or other methods of mucous clearance therapy can prevent the development of ACS in patients with SCD who have no chest-related symptoms, some centers advocate that IS/PEP or its equivalent should be started in all patients hospitalized with SCD regardless of the etiology.[10]

As our institution had also noted some patients with nonpulmonary symptoms progress to ACS, we sought to reduce the incidence of ACS and its complications through an evidence-based guideline (EBG) that drove the use of IS within clinical decision-support pathways. A recent study by Jayaram et al[11] showed that the implementation of a similar pathway for patients with SCD can dramatically increase compliance with mandated therapies, and that this has the potential to improve care and outcomes in this patient population. The goal of this study is to determine whether the use of mandatory IS will lead to a decreased incidence of ACS and associated complications when initiated from the emergency center (EC) for pediatric patients with SCD admitted for nonrespiratory complaints.

MATERIALS AND METHODS

This project received Institutional Review Board approval through Baylor College of Medicine. Texas Children's Hospital (TCH) is a large, urban, tertiary care pediatric hospital with over 85,000 outpatient EC visits per

Received for publication January 7, 2011; accepted April 8, 2011.
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None of the authors received financial support for this original work. The authors declare no conflict of interest.
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year. Almost 1000 patients with SCD are cared for by this facility. Approximately 95% of hospital admissions occur through the EC, where admission orders are generated for patients who are admitted to the inpatient wards. Before the creation of an EBG for SCD, there was wide variability in the management of children with SCD. The use of IS for patients with nonpulmonary complaints of SCD admissions was neither enforced nor tracked. The creation of interdisciplinary EBGs at TCH is done under the supervision of the Evidence-based Outcomes Center at TCH. This particular multidisciplinary EBG for SCD was created with input from multiple academic sections and service lines including Emergency Medicine, Hematology, Critical Care, Respiratory Therapy, Pharmacy, Nursing, and Child Life. Beginning on February 1, 2008 the EBG and companion order sets for SCD were implemented, thus integrating IS into routine care for all patients with SCD admitted from the TCH-EC. The only mandatory treatment codified in the EBG was the initiation of IS for all admitted patients with SCD regardless of reason for admission. It was to be started in the EC once the disposition was set for admission to account for potential delays in getting to the inpatient units. IS therapy was documented every 2 hours by a respiratory therapist from 8 am to 10 pm while hospitalized. IS was used in all patients from age 4 years and older; other options for those patients younger than 4 years or who were unable to perform IS were the use of PEP or soap bubble blowing at the discretion of the respiratory therapist. Before implementation of the EBG, IS was universally used in our institution for all patients with ACS, but its use in the remainder of patients with SCD without ACS or other respiratory symptoms was up to the discretion of the individual providers. The EBG also gave recommendations for adjunct therapies such as antibiotics, β agonists, glucocorticoids, and thresholds for packed red blood cell (PRBC) transfusions after the development of ACS in house if it occurred. However, the use of these additional interventions was left to the discretion of the treating physician of record. The EBG-defined ACS as an acute illness in patients with SCD associated with lower respiratory tract symptoms such as wheezing or rales, new hypoxemia, or a new infiltrate on chest radiography. This definition of ACS is what had been used before implementation of the EBG but was more formally codified in the EBG.

We conducted a retrospective cohort analysis of eligible patients admitted through the EC 1 year preintervention and 1 year postintervention of this EBG. We identified all patients evaluated in the EC with a diagnosis of SCD from February 1, 2007 to January 31, 2008 (the pre-EBG year) and February 1, 2008 to January 31, 2009 (the EBG year) using our hospital electronic medical record. Inclusion criteria were pediatric patients with SCD who presented to the TCH-EC without respiratory distress and who were admitted. Patients who presented with cough, chest pain, back pain, rib pain, or pleuritic pain were not excluded initially from review as these symptoms in isolation did not necessarily indicate active lung parenchymal disease and did not meet criteria for ACS. These patients without chest radiographs were still included in the study if they had no further documented signs of respiratory distress in the EC and no other indicators for ACS. Exclusion criteria were lower respiratory tract symptoms that the investigators believed were more likely to represent early ACS or lung parenchymal disease at presentation to the EC. These included a new infiltrate on chest radiography (if performed), wheezing or rales, tachypnea, increased retractions, or hypoxia relative to baseline. In addition, we also excluded patients who presented with lethargy, stroke, splenic sequestration, priapism, an aplastic crisis, or a history of receiving chronic transfusions. If there was a discrepancy between the investigators and attending physicians of record in determining whether a patient met criteria for ACS, the decision was made to defer to the final diagnosis given by the physician of record.

Patients who were admitted multiple times during the study period were enrolled and analyzed as independent admissions, as each hospitalization was considered a separate event in which ACS could develop. Demographic variables, chief complaints, and clinical findings were recorded. All statistical analysis was conducted using SAS 9.2, Cary, NC. One-way analysis of variance tests were used to compare continuous variables. Chi-square testing was used to compare categorical variables.

RESULTS

A total of 1551 patient visits to the TCH-EC were identified over the 2-year period. During this 2-year period, 833 EC visits resulted in admission. In the pre-EBG year, 258 patient visits (61%) were enrolled, whereas 230 patient visits (56%) were enrolled in the EBG year (Fig. 1). Forty-five percent of the enrolled patients had 1 visit per year of enrollment, with the majority (87%) having 4 or fewer admissions during each study period (range/year, 1 to 13). Patient demographics were similar in both years with no significant difference in age, sex, genotype, history of ACS, or recent admissions within the last 6 months (Table 1). Medication usage was very similar in both years, with the EBG year reporting a slightly higher use of hydroxyurea ($P < 0.01$) and oral analgesia ($P = 0.02$). Presenting complaints, vital signs, and laboratory values were similar between years as well, with a greater number of patients in the EBG year enrolled presenting with chest pain ($P = 0.03$) and headache ($P = 0.02$). The most common reasons for

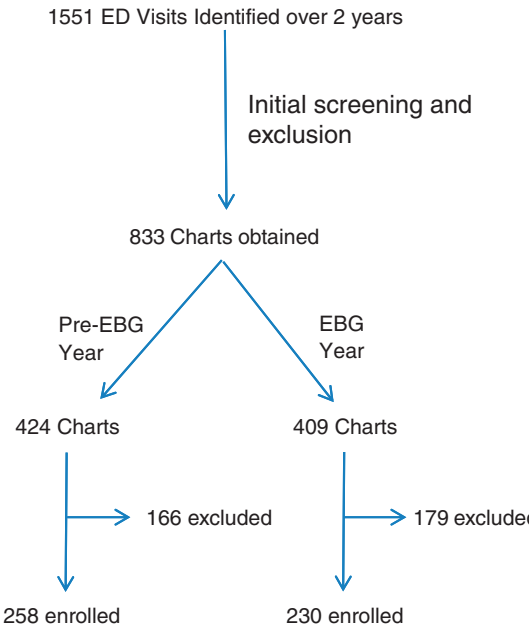

FIGURE 1. Patient flow diagram.

TABLE 1. Patient Characteristics

	Pre-EBG Year	EBG Year	
Enrolled Patients	**258**	**230**	***P***
Sex			N/S
Male	121	118	
Female	137	112	
Age in years (median)	10.3	12.8	N/S
Genotype (3 missing data points)			N/S
SS	205	185	
SC	34	25	
S-β	15	16	
S-other	1	4	
Initial vital signs			
Temperature (centigrade) (mean)	37.6	37.3	**< 0.01**
RR (mean)	24	22.5	**0.01**
O_2 Sat (%)	97.6	97.9	N/S
Chief complaint (some patients with multiple)			
Chest wall pain	32	44	**0.03**
Back pain	57	56	N/S
Headache	19	24	**0.02**
Fever	108	78	N/S
Cough	26	27	N/S
Pleuritic pain	6	6	N/S
Arm pain	51	49	N/S
Leg pain	91	81	N/S
Rib pain	2	3	N/S
Abdominal pain	50	43	N/S
WBC (median)	15.4	14.4	N/S
Hgb (median)	8.7	8.9	N/S
Retic (median)	9.1	8.7	N/S
History of ACS	92	99	N/S
Admissions within last 6 mo	161	126	N/S
On chronic medications			
PenVK	180	151	N/S
Folate	206	171	N/S
Hydroxyurea	31	48	**< 0.01**
Desferoxamine	0	3	N/S
Analgesic	106	119	**0.02**

ACS indicates acute chest syndrome; EBG, evidence-based guideline; WBC, white blood cells.

exclusion were hypoxemia relative to baseline (50% of excluded patients) or the presence of a new infiltrate on chest radiograph whereas in the EC (46% of excluded patients). Many patients had more than 1 complaint at presentation. Overall, of the 345 patients excluded, 72% had at least 1 respiratory complaint on presentation, with most having multiple respiratory complaints.

As all patient charts were reviewed it was confirmed that all patients with a diagnosis of ACS received PRBCs during the 2-year study period. From year 1 to year 2 a statistically significant decrease was seen in development of an oxygen requirement ($P < 0.01$) and in need for antibiotics ($P = 0.01$). Overall length of stay was similar between years (4.8 vs. 4.64 d, NS), as well as the need for exchange transfusions (4 vs. 2, NS) and ICU utilization. Sixty-seven patients (25.9%) in the pre-EBG year received transfusions versus 51 patients (22.5%) in the year following its initiation (NS). Twenty-five patients (9.6%) in the pre-EBG year received PRBCs for ACS versus 14 (6.1%) in the EBG year (absolute risk reduction: 3.5%, 95% confidence interval: −1-8.4%) (Table 2). When the patient complaints were analyzed as risk factors for needing transfusions, it was found that back pain and chest pain were associated with an increased risk of needing PRBC transfusions. Subgroup analysis of patients who presented with these and other symptoms (Table 3) revealed a statistically significant decrease in the number of patients with back pain who were later diagnosed with ACS and received PRBCs with back pain. There were 13 of 57 patients in the pre-EBG year and 5 of 56 patients in the EBG year ($P = 0.04$, absolute risk reduction: 14%, 95% confidence interval: 1-28%; number needed to treat: 8). As hydroxyurea usage was greater overall in the EBG year, we compared the usage of it in patients who needed transfusions or who developed ACS in both years to determine if its usage affected the reduced incidence of ACS. No difference was found in either one of these groups or in the subgroup of those who presented with back pain alone, indicating the early and mandatory introduction of IS seems to be responsible for the decrease seen in the development of ACS in the EBG year.

DISCUSSION

IS is used in patients with SCD to help prevent atelectasis and to encourage good lung aeration despite splinting secondary to pain. Prior studies by Bellet and Hsu[8,9] in children and adults have shown that using IS or PEP can prevent progression of pulmonary disease in those experiencing chest or back pain or pulmonary symptoms;

TABLE 2. Patient Outcomes

	Pre-EBG Year	EBG Year	
Enrolled Patients	**258**	**230**	***P***
Received IV fluids—no. (%/y)	232 (89.9)	213 (92.6)	N/S
Oxygen needed—no. (%/y)	40 (15.5)	8 (3.5)	< 0.01
Antibiotics given as inpt—no. (%/y)	149 (57.8)	106 (46.1)	< 0.01
CXR obtained—no. (%/y)	164 (63.6)	151 (65.6)	N/S
Total PRBC transfusions—no. (%/y)	67 (26)	51 (22.5)	N/S
Cases of ACS—no. (%/y)	25 (9.6)	14 (6.1)	N/S
PRBC for ACS—no. (%/y)	25 (9.6)	14 (6.1)	N/S
Exchange transfusion needed—no. (%/y)	4 (1.5)	2 (0.9)	N/S
PICU stay (d)	0.06	0.24	N/S
Overall hospital stay (d)	4.8	4.64	N/S

ACS indicates acute chest syndrome; EBG, evidence-based guideline; PICU, pediatric intensive care unit.

TABLE 3. Patient Symptoms, Transfusion Requirements, and Development of ACS

	Pre-EBG Year	EBG Year	*P*, ARR, 95% CI
Back pain (no. patients)	57	56	
CXR at admission (%)	37/57 (65)	43/56 (77)	
No. receiving any transfusion (%)	23/57 (40)	13/56 (23)	**0.05, ARR 17%, 95% 0-34**
No. developing ACS in house (%)	13/57 (23)	5/56 (9)	**0.04, ARR 14%, 95% 1%-28%**
Fever	108	78	
CXR at admission	76/108 (70)	63/78 (81)	
No. receiving any transfusion	25/108 (23)	20/78 (26)	N/S
No. developing ACS in house	4/108 (4)	3/78 (4)	N/S
Chest pain	32	44	
CXR at admission	31/32 (97)	40/44 (91)	
No. receiving any transfusion	13/32 (41)	19/44 (43)	N/S
No. developing ACS in house	5/32 (16)	6/44 (14)	N/S
Cough	26	27	
CXR at admission	22/26 (85)	22/27 (81)	
No. receiving any transfusion	11/26 (42)	6/27 (22)	N/S
No. developing ACS in house	5/26 (19)	2/27	N/S
Pleuritic pain	6	6	
CXR at admission	5/6 (83)	6/6 (100)	
No. receiving any transfusion	2/6	0/6	N/S
No. developing ACS in house	0	0	N/S
Rib pain	2	3	
CXR at admission	2/2 (100)	3/3 (100)	
No. receiving any transfusion	1/2	2/3	N/S
No. developing ACS in house	1/2	2/3	N/S
Leg pain	91	81	
CXR at admission	56/91 (61)	54/81 (67)	
No. receiving any transfusion	17/91 (19)	16/81 (20)	N/S
No. developing ACS in house	9/91 (10)	4/81 (5)	N/S
Arm pain	51	49	
CXR at admission	35/51 (69)	31/49 (63)	
No. receiving any transfusion	6/51 (12)	6/49 (12)	N/S
No. developing ACS in house	2/51 (4)	1/51 (2)	N/S
Abdominal pain	50	43	
CXR at admission	34/50 (68)	24/43 (56)	
No. receiving any transfusion	8/50 (16)	5/43 (12)	N/S
No. developing ACS in house	5/50 (10)	2/43 (5)	N/S
Headache	19	24	
CXR at admission	15/19 (79)	18/24 (75)	
No. receiving any transfusion	5/19 (26)	8/24 (33)	N/S
No. developing ACS in house	2/19 (11)	3/19 (16)	N/S

Total numbers are greater than enrolled as some patients had more than 1 presenting chief complaint.
ACS indicates acute chest syndrome; ARR, absolute risk reduction; CI, confidence interval; EBG, evidence-based guideline.

however, no studies have investigated its direct impact in the prevention of ACS or its complications among those SCD patients with other symptoms. Studies using IS in other context, such as the postsurgical patient, has shown that it can prevent atelectasis.[12] This study has examined the efficacy of mandatory IS in the management of SCD patients admitted with nonpulmonary complaints of SCD to prevent the development of ACS. This study not only showed a decrease in the development of ACS for all patients, but a statistically significant decrease for those patients who presented with back pain and no other respiratory symptoms. There was also a decreased need for oxygen use, antibiotic use, and in PRBC transfusions for ACS for patients presenting with back pain. In the EBG year there was a concomitant increase in PRBC transfusions for non-ACS reasons, but the reason for this is not clear from our study data and outside the scope of this study.

Back pain in patients with SCD may have different etiologies; it may be from vaso-occlusive crises from the thoracic skeleton, the intercostal muscles, the pleural lining of the cavities, or the lung parenchyma itself, which would manifest as ACS. Back pain from nonpulmonary etiologies could certainly predispose a patient to splinting and hypoventilation. This could lead to an increased risk of atelectasis and V/Q mismatch and subsequent ACS development; hence, the importance of the use of pulmonary interventions such as IS to prevent this possibility. A significant percentage of enrolled patients who presented with back pain and no other respiratory symptoms did not obtain chest radiographs at presentation, raising the possibility of a subclinical or presymptomatic ACS being missed. Although it is not standard practice to obtain chest radiographs on all SCD patients with isolated back pain, it was difficult to determine from this retrospective chart review the exact reasons the treating physicians chose to obtain or defer a radiograph. We looked at the hospital course of those patients who did not have radiographs obtained at EC presentation. Two of 20 patients in the first year developed ACS several days later in their hospital course, and none of the 13 patients in the second

year did. This suggests the treating physician judgment was likely correct in determining that there was not an active pulmonary etiology for the back pain, instead arising from a nonpulmonary source for which the mandatory IS would help prevent splinting and other milieu for ACS to develop.

The pathophysiology of ACS includes a variety of precipitating factors, such as infection and fat emboli, that may have an unclear role in standardizing therapy. Standard management of ACS entails the use of IS to prevent further alveolar collapse, though it will likely not have a strong effect in those patients with that predominantly have ACS due to infection or fat emboli. It is plausible that the use of spirometry would decrease the need for oxygen use, regardless of any other symptoms, as patients who are bed-ridden due to pain or other severe illness may have poor inspiratory efforts even if they do not have severe chest pain or a primary pulmonary process. In our study, as the number of patients admitted for fever, which necessitates antibiotics, remained similar, the decreased overall need for antibiotics is likely a reflection of fewer infiltrates seen on chest radiograph due to fewer cases of atelectasis and hypoxemia. There was a decrease in the number of patients developing ACS needing multiple PRBC transfusions, a possible measure of severity of illness, but our study was not powered to detect this difference. Although a cost/benefit analysis would be relevant to impact within the healthcare infrastructure, it is beyond the scope of this study.

It is unclear why there was a statistically significant difference in the use of analgesics in our 2 study years as there was no known significant change in practice regarding analgesic use during the study period. Inpatient use of narcotics was not tracked specifically in this study, but further studies that look at the type of narcotic given (morphine vs. fentanyl) or administration method (as needed vs. continuous patient controlled analgesia) affecting the development of ACS would be important.

There was a shift toward increasing the usage of hydroxyurea during the study time by our hematology division, but an analysis controlling for the use of hydroxyurea indicates this was not the reason for the decreased incidence of ACS between the 2 years. During our individual chart review, over 70% of exclusions occurred due to respiratory symptoms that were concerning for ACS in the EC. Whether this is because the patients are waiting too long for evaluation, are having quickly progressing symptoms before presentation, or is simply a reflection of our population is unknown and bears a need for further study.

By focusing on many objective measures for inclusion/exclusion and outcomes we were able to ameliorate some of the limitations of the retrospective design. In our institution, only 5% of admissions bypass the EC, thus limiting the population that could be studied outside the EC's EBG as a comparison group. We did not formally evaluate the nursing and respiratory therapists' documentation of IS compliance and frequency of use in the pre-EBG year, but an unrelated parallel study at our institution showed close to 100% documentation of compliance of IS in the EBG year. Continued implementation of EBGs and reinforcement of their use with staff will continue to increase the rate of compliance. The overwhelming majority of patients received IS, but compliance with IS in the patient less than 5 years of age is very difficult, at times perhaps requiring other forms of atelectasis prevention. From this retrospective chart review, documentation of the exact technique used for these young patients was not always clearly documented. Regardless, most providers would believe that atelectasis prevention is paramount, and the method by which it is achieved being of secondary importance. In this young group, determining whether IS is superior to bubble blowing or PEP therapy may be impossible to determine. As there were a few cases of ACS in this group (2 in the pre-EBG year and 4 in the EBG year), efforts to include them was important as well. Some of the patients receiving multiple transfusions had ongoing anemia, and the retrospective nature of the study limited our ability to determine if the additional transfusions were done primarily for ongoing ACS symptoms or for anemia alone. There were 5 patients (3 in the pre-EBG year and 2 in the EBG year) who met the EBG definition for ACS, but did not receive PRBCs and were not diagnosed with ACS by their treating physician. To avoid confusion and statistical misinterpretation, the investigators' chose to defer to the diagnosis given by the treating physician at the time of treatment rather than try to assign ACS from the information gleaned from a retrospective chart review.

In conclusion, the use of IS among children admitted for SCD with nonpulmonary complaints reduces the risk of developing ACS and the associated need for oxygen therapy, antibiotics in all patients, and reduces the need for transfusions in patients presenting with back pain. Its use should be very strongly encouraged for those patients who are admitted with back pain as this cohort is not only at high risk for progression to ACS but seems to receive the greatest benefit from its mandatory utilization.

ACKNOWLEDGMENT

The authors thank the members of the Ad hoc team that designed the EBG: Michelle Mariscalco, MD; Gladstone Airewele, MD; Suzanne Iniguez, RT; Lee Evey, RT; Julie Katkin, MD; Joy Hesselgrave, RN; Elizabeth Fredboelling, RN; Tangula Taylor, RN; Shelly Oh, PharmD; Joseph Y. Allen, MD; Mireya Velasquez, MD; and Co-Chairs Marilyn Hockenberry PhD, RN, PNP-CS, FAAN; and Virginia Moyer MD, MPH. The authors also thank Long Ma for his statistical work and the members of the Center for Clinical Effectiveness for their support of this project.

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