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A Mixed-Methods Study of Pain-related Quality of Life in Sickle Cell Vaso-Occlusive Crises

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Abstract

The quality of care for sickle cell disease patients hospitalized with a vaso-occlusive crisis (VOC) is poor, resulting in staggeringly high healthcare resource utilization. To evaluate in-patient care for VOC, we conducted a mixed-methods study of all adult sickle cell disease patients admitted with a VOC from 2010–2012. We quantitatively assessed the quality of care for all patients, and qualitatively studied a subset of frequently admitted patients. In total, there were 182 admissions from 57 unique patients. The median length of stay was 6 days and the 30-day readmission rate were 34.0%. We identified red blood cell transfusion and patient controlled analgesia use as predictors of increased length of stay. Interestingly, unlike prior findings, younger patients (18–30 years old) did not have increased healthcare resource utilization. Moreover, older age appeared to increase readmission rate and enhance the effect of patient-controlled analgesia use on length of stay. Interviews of high healthcare resource utilizers revealed significant deficiencies in pain management and a strong desire for individualized care. This is the first study to examine in-patient predictors of acute healthcare resource utilization in sickle cell disease patients and to correlate them with qualitative perspectives of high healthcare resource utilizers.

Keywords

Healthcare resource utilization; pain; quality of care; sickle cell disease; vaso-occlusive crisis (VOC)

Introduction

Sickle cell disease is a lifelong hemoglobinopathy producing chronic hemolytic anemia, microvascular thrombosis, ischemic pain, tissue infarction, decreased quality of life, and ultimately, shortened life expectancy (1). Recurrent painful crises are thought to result from transient episodes of microvascular congestion, tissue ischemia, and the release of inflammatory mediators (2). The mechanism of acute pain in these vaso-occlusive crises

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Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of this article.

(VOCs), is related to a combination of ischemic tissue damage, hypoxia/reperfusion injury, and inflammation, and may have both somatic and neuropathic components (2,3). The pain associated with such episodes is variable, but maybe excruciatingly severe and functionally disabling (4).

These recurrent episodes of VOCs account for more than 100,000 hospital admissions annually in the United States at a cost of more than US\$2 billion (5,6), even though most individuals manage these crises at home with sporadic admissions occurring, on average, 1.5 times per year (7). Of note, some VOC admissions use an inordinate amount of healthcare resources due to prolonged length of stay and frequent readmission to the hospital (7–10). In a landmark study of one-third of the US population with sickle cell disease, younger patients (18–30 years old) and patients with public insurance appear to utilize healthcare resources the most, averaging 3.6 acute care encounters per year and a 30-day readmission rate of more than 40.0% (10). While it is possible that those with the severest disease die at a younger age, thus accounting for the above findings (7), it is also possible that there is a poor transition from pediatric to adult care (11). Additionally, a subgroup of patients is admitted frequently, as often as several times per month, over successive years, and account for a disproportionately high share of total costs (12,13). Three or more hospital admissions per year have been correlated with a lower 5-year survival rate (14). Rehospitalization within 30 days has emerged as a clinical indicator of the quality of care for many diagnoses (15) and has recently been adopted as a quality indicator for sickle cell care (16). While hydroxyurea (HU) is the only proven therapy to reduce hospital admissions, length of stay, and analgesic use, it is still vastly under-utilized (1,17,18).

To determine the actual pattern of hospital admissions, length of stay, and pain experiences of sickle cell disease patients with VOC and causes of their frequent readmissions, we conducted a mixed-methods cohort study of all adult sickle cell disease patients admitted with a VOC during a 2-year period. Our study is the first to correlate in-patient predictors of acute healthcare resource utilization in sickle cell disease patients admitted with a VOC with unique, qualitative perspectives of identified high healthcare resource utilizers.

Materials and methods

Between July 1, 2010 and June 30, 2012, we conducted a retrospective cohort study at our institution, a large urban academic medical center. The institutional review board approved all study protocols, survey instruments, and interview templates (available upon request). All adult patients age 18 years or older admitted with a VOC identified through ICD-9 codes were included in the study (57 patients, 182 admissions). We used standardized procedures to collect data from the hospital's electronic health record on demographic and clinical characteristics, including hemoglobin (Hb) subtype, age at time of admission, gender, current HU use, documented primary care physician, documented hematologist, the use of patient controlled analgesia (PCA), transfusion of red blood cells, length of stay, documented follow-up appointment on discharge, and whether readmitted within 30-days of discharge to the same institution. Visits to the emergency department without inpatient admission were not included. Because hospitalizations were clustered within individual patients, we used hierarchical linear models with robust standard errors to assess both patient

and hospitalization effects on length of stay. We used hierarchical logistic regression to assess for predictors of 30-day readmission, adjusting for clustering within individual patients. All analyses were conducted using Stata software, version 12 (StataCorp, College Station, TX, USA).

We approached the group of 15 high healthcare resource utilizers (>3 admissions/year) and requested interviews; nine (60.0%) were available and agreed after investigators obtained written consent. The interview template included open-ended questions focusing on patients “experience living with sickle cell disease, pain management experience in the hospital, and circumstances of frequent hospital admissions” (available upon request). Finally, participants were encouraged to freely express their opinions on best practice. Emerging themes were further pursued and clarified using the technique of cognitive interviewing (19). Two investigators (RJL and KW) performed independent coding of qualitative interview transcripts and thematic analysis to identify common patterns and theories based on matrices of responses and constant comparisons. Throughout the iterative process, codes and themes were reviewed for agreement and disagreement, and discussed for consensus (19).

Results

During the 2-year study period, 57 patients with sickle cell disease were admitted 182 times for VOC (average 3.2 admissions per patient) (Table 1). The median age was 35 years, 61.0% were female, and 61.0 and 21.0% had Hb S (*HBB*: c.20A>T) and Hb SC (*HBB*: c.19G>A) genotypes, respectively. Twenty-five patients had only one admission, but 15 patients had more than three admissions each during the period and accounted for 64.0% of total admissions (117/182). The median length of stay was 6 days (interquartile range 3–10 days), and the likelihood of readmission within 30 days of discharge was 34.0% (Table 1). Overall, PCA was used in 14.0% of hospitalizations and transfusion of red blood cells occurred in 33.0%. Hydroxyurea use was documented as an outpatient medication for 67 (37.0%) of the 182 hospitalizations. For less than half of hospitalizations did the patient have a documented primary care physician or a hematologist (Table 1). Hemoglobin genotypes did not have an effect on length of stay (data not shown). When tabulated according to two age groups, age 18 to 30 (one-third) and age >30 (two-thirds), both groups had similar composition of female, Hb S genotype, and average numbers of hospitalization. However, older patients tended to stay longer with median length of stay of 6 days as compared to 5 days, and were readmitted more frequently, 38.0 vs. 22.0%, although the differences were not statistically significant (data not shown).

Among all variables, there were significant associations in three outpatient care variables, use of HU, having a hematologist, and having a primary care physician ($p < 0.001$, χ^2). In univariate analysis, the strongest predictors of length of stay included use of PCA (extra 8.6 days) and the transfusion of red blood cells (extra 5.2 days) (Table 2). In multivariable analysis, patient age modified the effects of PCA use on length of stay but did not modify the effects of red blood cell transfusions. As shown in Table 3, in younger patients (age 18–30 years old), PCA use prolonged length of stay by 3.8 days, while in older patients (age 30 and above), the effect was greater (increase in length of stay by 12.8 days; $p = 0.007$ for interaction of age and PCA use). Transfusion of red blood cells ($p = 0.004$) remained

statistically significant in the multivariable model. None of the demographic or clinical variables were significant multivariate predictors of 30-day readmission rate (all $p > 0.20$). When dichotomized by age, older patients (age 30 and above) appeared to have higher rate of readmission as compared to the younger group, 38.0 vs. 22.0%. However, it was not statistically significant after adjusting for clustering (data not shown). In addition, 12 of the 15 high healthcare resource utilizers were older than 30 years.

Dominant themes of the interviews with nine of the 15 patients with at least three hospitalizations fell into six categories: (1) adverse impacts of chronic sickle cell pain, (2) poor HU use, (3) reluctance to accept PCA, (4) reluctance to accept a standard protocol, (5) unpredictability of hospital readmission, (6) age and morbidities. Most patients described prolonged emotional, psychological and functional morbidity from their sickle cell anemia and its associated chronic pain and other complications. They also described a nearly uniform sense of helplessness and frustration in predicting VOC occurrence, described by one patient as a “living hell.” There was a common perception that HU was difficult to take, and a common distaste for PCA and standardized protocols for pain management. Most participants cited past experience with inadequate control as the main reason. For example, “(I am) a little paranoid because of bad experiences I’ve had in the past,” and “I stick with what I know works for me.” In addition, lack of understanding of these treatment modalities was apparent, especially for PCA. For example, many patients dismissed PCA as inadequate for treating their pain, or possibly dangerous: “getting it in little bits by pressing the button,” and “everybody says that it’s not too good to be on it for too long.” Additionally, these interviews highlighted the unpredictable nature of readmissions, for example, “sometimes it just happens,” and “I don’t have that luxury to go home and rest.” Finally, these interviews described increased complications from sickle cell anemia, which contributed to morbidities and patient-perceived acute health care resource utilization, for example, “got worse as I got older,” and “a lot of big stuff has happened to me.”

Discussion

Despite the increased life expectancy of sickle cell disease patients over the past several decades, they still suffer significant mortality and morbidity due to long-term complications of sickle cell disease and significant psychosocial burdens associated with acute and chronic pain (20). In this study, we characterize the experiences of sickle cell anemia patients hospitalized with a VOC. Their high disease burden was reflected by a median length of stay of 6 days as compared to the national expected length of stay of 4 days and actual length of stay of 5–6 days (18,21), and a 30-day readmission rate of 34.0% as compared to the national average of 30.0–40.0% (10). A small percentage of patients, 15 (26.0%), accounted for a disproportionately high percentage of all admissions (64.0%), a finding corroborated by previous studies and again suggests that targeting these high healthcare resource utilizers may help reduce care burden (9,12). Despite evidence supporting PCA use to treat acute pain in VOC (22), it occurred infrequently (14.0% of hospitalizations), consistent with a major theme from our interviews with patients that PCA was perceived as unreliable and less desirable than alternative methods for controlling pain. When PCA was used, however, there was an associated prolonged length of stay in excess of 8 additional days (nearly 4 extra days in patients age 18–30 years and nearly 13 extra days in patients over age 30 years old).

The reason for this association is unclear. One possibility is that PCA was less effective in controlling pain, as suggested by the patients interviewed, and inadequate pain control prolonged the VOC. An alternative explanation was that PCA use was a marker for either patient or provider characteristic that was the underlying cause of the prolonged length of stay. In addition, we found that red blood cell transfusion was associated with increased length of stay, meaning that the need for a blood transfusion was also a marker for more severe episodes of VOC.

In contrast to prior studies, which showed that younger patients (age 18–30 years) tended to use more health care resources that was attributed to early death of more severe sickle cell disease patients or inadequate pediatric-to-adult transition of sickle cell care (10,11,23), in our study there were no significant differences between age groups, and in fact, PCA use in older patients prolonged length of stay much more than in younger patients and admissions from older patients also tended to lead to more 30-day readmissions (38.0 vs. 22.0%). In addition, Hb genotypes did not affect the result of our analysis. It is possible that there is accumulation of more serious complications and comorbidities and/or decreased responsiveness to classic sickle cell treatments such as HU or PCA in older sickle cell disease patients, which is additionally supported by themes from our qualitative interviews.

Our qualitative study elucidated pain management and hospitalization experiences among high healthcare resource utilizers. The long-term, disabling impact of sickle cell disease was apparent, as well as the consequences of frequent VOC and associated acute on chronic pain. Under-treatment of pain and lack of education on pain management in the hospital, especially on PCA, were common themes, although perceived opioid addiction was less worrisome from the patients' perspectives. Additionally, these high healthcare resource utilizers tended to oppose a standard VOC management protocol. The strong preference for individualization of VOC care is a unique theme, not previously appreciated in the literature, and needs to be explored further. Psychologically, individualized care may give these suffering patients a strong sense of control and reduce their stress levels. Similar to our quantitative results, the hospital readmission was unpredictable from these patients' perspectives. Compared with previous qualitative studies, our findings revealed more concerns with clinical approaches to pain management and patient education, and fewer psychosocial issues complicating hospitalization and readmissions (24,25).

Our study is limited by its single center study design, small sample size, and the lack of capability to extract individual pain-related data, social-economic status, and types of insurance from the electronic health record. Given the small cohort, our qualitative interview may not have achieved thematic saturation. Despite these limitations, our quantitative findings are generally consistent with published observational data (6–13,17,21), and our qualitative analyses expand the scope of insights for this historically difficult-to-manage patient population (16,17,26). Our inability to identify multivariate predictors of 30-day readmission suggest that either our sample size is too small or yet unmeasured clinical and psychosocial factors may contribute, for example, high outpatient pain score as suggested by a recent study (23).

Conclusions

Our results indicate an urgent need for improving in-patient VOC pain management in sickle cell disease patients and call for innovative care models encompassing longitudinal collaborations among hematologists, pain and palliative care specialists and community-based home health agencies in order to reduce the chronic suffering and the staggering healthcare resource utilization (27). Given the significant pain, comorbid complications, and severely impaired quality of life associated with sickle cell anemia (26), a chronic disease management model involving palliative care will not only address the patient's physical illness but also the social, psychological, and emotional components that play a significant role in frequent exacerbations of their disease (28). Indeed, these patients need palliative care from birth (29).

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Table 1.

Characteristics of adult patients with sickle cell anemia hospitalized for a vaso-occlusive crisis from 2010 through 2012.

Patient Characteristics	<i>n</i>	%
Patients	57	
Females	35	61.0
Hb S (<i>HBB</i> : c.20A>T)	35	61.0
Age median (IQR) (range) (years)	35 (28–42) (18–63)	
Number of hospitalizations per patient		
Median (IQR) (range)	5 (2–11) (1–26)	
\$ 1 hospitalization (<i>n</i>) (patients)	25 (25)	
\$ 2 hospitalizations (<i>n</i>) (patients)	22 (11)	
\$ 3 hospitalizations (<i>n</i>) (patients)	18 (6)	
\$ >3 hospitalizations (<i>n</i>) (patients)	117 (15)	
Hospitalization Characteristics		
\$ number of hospitalizations (<i>n</i>)	182	34.0
\$ length of stay median (IQR) days	6 (3–10)	14.0
\$ 30-day readmission <i>n</i> (%)	61	33.0
\$ PCA use during hospitalization <i>n</i> (%)	25	54.0
\$ red blood cell transfusions <i>n</i> (%)	60	47.0
\$ follow-up appointments made <i>n</i> (%)	99	45.0
\$ primary care physician documented <i>n</i> (%)	85	37.0
\$ hematologist documented <i>n</i> (%)	82	
\$ HU use <i>n</i> (%)	67	

IQR: interquartile range; PCA: patient controlled analgesia; HU: hydroxyurea.

Table 2.

Univariable predictors of hospital length of stay.

Predictor	Effect Size (days)	<i>p</i> Value
PCA use	+8.6	<0.001
Red blood cell transfusions	+5.2	0.001
Follow-up appointment made	+1.7	0.05
Age >30 years	+0.7	0.61
Having a primary care physician	+0.6	0.65
Females	−2.1	0.21
HU use	−1.4	0.39
Having a hematologist	−0.8	0.60
Hb S (<i>HBB</i> : c.20A>T)	−0.8	0.63

PCA: patient controlled analgesia; HU: hydroxyurea.

Table 3.

Multivariable predictors of hospital length of stay by age group. [No significant 3-way interaction between age group, transfusions and PCA use ($p = 0.2$)]

Age Group	18–30 Years	>30 Years	<i>p</i> Value
Predictor (Effect size in days)			
Baseline (no transfusion or PCA use)	7.4	9.0	0.77
Red blood cell transfusions	+5.7	+5.7	0.004 ^a
PCA use	+3.8	+12.8	<0.001 ^b

PCA: patient controlled analgesia.

^aNo significant interaction between age group and transfusion ($p = 0.18$).

^bSignificant interaction between age group and PCA use ($p = 0.007$).