HEMOGLOBINS
Making an evolutionary perfected process, imperfect
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PLENARY SESSION – SATURDAY, APRIL 29, 2017

**JSCDH-D-17-00019: Heme Promotes Pulmonary Hypertension in SCD by Inducing Secretion of Placenta Growth Factor from Erythroblasts via Oxidant Response Transcription Factors**

**Authors:** Oluwabukola T. Gbotosho, Maria G. Kapetanaki, Deva Sharma, Valerie Schrott, Frances Weidart, Solomon Ofori-Acquah, Grant Bullock, and Gregory J. Kato.

**Affiliations:** Division of Hematology-Oncology, Department of Medicine and the Heart, Lung and Blood Vascular Medicine Institute, and Division of Hematopathology, Department of Pathology, University of Pittsburgh School of Medicine.

**Abstract**

**Background:** Patients with sickle cell disease (SCD) have elevated plasma levels of placenta growth factor (PIGF) which promotes expression of the pulmonary vasoconstrictor endothelin-1 (ET-1) contributing to pulmonary hypertension, an important age-related and life-limiting complication of SCD. In SCD patients, markers of high iron burden are associated with the highest PIGF levels, leading us to hypothesize a mechanistic link between excessive iron and the induction of the PIGF protein.

**Methods:** We have established *in vitro* models of heme-bound iron (hemin) stimulation of the PIGF promoter in human K562 cells and in primary human erythroid cells. With the use of real time PCR, we have assessed the transcriptional regulation of several genes involved in the NRF2 antioxidant response pathway as well as their contribution to PIGF and HO-1 transcriptional regulation. We have established a murine primary bone marrow cell culture model and an *in vivo* murine model of PIGF response to heme exposure.

**Results:** Gene expression knockdown and small molecule inhibitor and activator experiments demonstrate a central role of NRF2 in activating the PIGF promoter in response to heme, supported by chromatin immunoprecipitation experiments. The PIGF promoter is robustly activated by a well characterized non-oxidative NRF2 agonist (Sulforaphane) and by the nonspecific oxidant hydrogen peroxide, while it is inhibited by an NRF2 inhibitor (Brusatol), by siRNA directed against NRF2 and by the nonspecific antioxidant N-acetyl cysteine. We also find that NRF2 activation regulates the transcript levels of several other NRF2 family members. PIGF induction overlaps with HO-1 regulation except that PIGF is apparently not regulated by BACH-1. Finally, we have confirmed that intravenous injection of heme in wild type mice induces PIGF mRNA expression in bone marrow, and secretion of PIGF protein into blood within three hours. This response is dramatically blunted in mice deficient in NRF2, further supporting the importance of NRF2 in heme induction of PIGF expression *in vivo*. Conclusions: Our results to date support a mechanism in which accelerated heme turnover in SCD promotes robust
expression of PlGF in erythroblasts during erythroid differentiation, through a pathway that involves EKLF, NRF2 and MaF. This mechanism helps to explain the clinical observation that heavily transfused, iron overloaded adults with SCD are more likely to develop pulmonary hypertension, as a potential consequence of excess heme trafficking from the turnover of transfused red cells. These results might inspire greater adherence to existing approved therapies to chelate iron in SCD.

JSCDH-D-17-00036: Visual Explorer: Using Pictures to Facilitate Dialogue on Complex Sickle Cell Disease Issues

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Abstract

Background: Visual Explorer (VE) is a tool that uses images with framing questions to explore complex issues from a variety of perspectives. Communication is essential to build trust between patients with sickle cell disease (SCD) and healthcare providers; however, SCD patients have reported difficulty communicating with their providers. VE uses images to help facilitate discussion of sensitive issues and overcome barriers.

Method: Twenty attendees of the 3rd Annual SCD Patient and Family Symposium participated in the exercise; 10 SCD patients/4 caregivers/4 spouses/significant others/2 SCD providers (14 female; 6 males). The participants were divided into 3 groups each led by a SCD nurse facilitator. The exercise used 6” x 4” VE image cards with 54 cards per deck. One image deck was displayed on the table in front of each group. All participants were given a framing question and asked to select an image that represented the answer to the question. After selecting a card, each participant displayed their card to the group and explained the relationship between their answer to the question and the VE image.

Results: Responses to the framing question: “How do you feel when you are in acute pain/your loved one is in acute pain/you are treating someone in acute pain” had a common theme from each group and the diverse populations (SCD patients, caregivers/significant others, and providers); the theme was discrimination. One caregiver displayed a picture of a momma bear attacking and said it represented her fight to get care for her loved one, and that she would never give up. A SCD patient displayed a picture of a person climbing a steep wall and stated it represented a never-ending uphill battle; a SCD provider displayed a picture of a group holding up hands stating he wanted to
tell his colleagues to “hold up” because he felt like he was scrutinized more closely when he treated patients with SCD. Each image led to a deeper discussion of the issue and input from other group members. The session lasted 2 hours.

**Conclusion:** SCD involves complex subjects of discussion including medical, emotional, and psychological issues that must be addressed by the healthcare provider. VE helps facilitate discussions to help reach a shared understanding of these complex issues.

**JSCDH-D-17-00018: Changes in Exploratory Biomarkers in a Phase 1B, Randomized, Double-Blind, Placebo-Controlled Study of PF-04447943 in Patients with Stable Sickle Cell Disease**

**Authors:** David Beidler, PhD; Michael Messig, PhD; Robert J. Charnigo, MS; Debra Pittman, MS; Denis Rybin, PhD; Krupa Sivamurthy, MD; Beesan Tan, PhD; Mehri Afsharvand, PharmD; Alan D. Michelson, MD; Andrew L. Frelinger, PhD; Nicholas Clarke, PhD

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**Abstract**

**Background:** Sickle cell disease (SCD) is caused by a single amino change in the β-globin gene and is characterized by a complex and heterogeneous pathophysiology. Currently, no validated biomarkers for SCD exist. We sought to explore biomarkers that may be informative in demonstrating the pharmacologic effect of PF-04447943, a selective inhibitor of the cyclic guanosine monophosphate (cGMP)–specific phosphodiesterase-9A enzyme in clinical development for the prophylactic treatment of SCD.

**Methods:** This phase 1b, multinational, multicenter, double-blind, placebo-controlled study enrolled adults aged 18–65 years with stable SCD (hemoglobin [Hb]SS or HbS-β0 thalassemia) with and without the co-administration of hydroxyurea. Patients were randomized 3:1 to receive twice-daily (BID) PF-04447943 5 mg, PF-04447943 25 mg, or placebo. The safety and tolerability of PF-04447943, the primary objective of this study, are presented separately. Exploratory endpoints included change from baseline at day 29 in plasma cGMP; markers associated with cellular adhesion; monocyte- and neutrophil-platelet aggregates percent and size; macrophage-1 antigen expression on monocytes and neutrophils; markers associated with coagulation; circulating endothelial microparticles; and HbF. Changes from baseline were analyzed using repeated measures analysis of covariance models, adjusting for the baseline in each dose group separately. A biomarker change from baseline was considered statistically significant if the
Holm step-down adjusted $P$ value was <.15.

**Results:** In total, 28 patients received study drug and had available biomarker assessments. In the PF-04447943 25-mg BID cohort (n=14), significant reductions from baseline to day 29 were observed for soluble E-selectin (-11%, $P=.064$), neutrophil-platelet aggregate numbers (-46%, $P=.095$) and size (-34%, $P=.018$), and monocyte-platelet aggregate numbers (-52%, $P=.025$) and size (-36%, $P=.140$). Similar trends were observed in the PF-04447943 5-mg BID cohort (n=7), but only the change in neutrophil-platelet aggregate size (-43%, $P=.020$) was significant. No significant change from baseline was noted at day 29 in plasma cGMP or HbF levels in either PF-04447943 cohort. No significant change in any biomarker was observed in the placebo cohort (n=7). An analysis of patients with and without hydroxyurea co-administration showed similar trends in biomarker activity.

**Conclusions:** Changes in the exploratory biomarker panel observed in this phase 1B study of PF-04447943 in patients with stable SCD are similar to those previously observed in preclinical SCD mouse models and with rivipansel administration in a pilot study of patients with SCD. The findings of this study provide insight into the mechanism of action of PF-04447943 and guidance for relevant biomarkers in future clinical studies.

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**BREAKOUT SESSION I- SUNDAY APRIL 30, 2017**

**PSYCHOSOCIAL**

**JSCDH-D-17-00021: Hospital admissions, mortality and comorbidities among New York State sickle cell patients, 2005-2013**

**Authors:** Elizabeth Linton MPH,1,2 Arielle L Langer MD MPH,3 Jeffrey Glassberg MD MA

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**Abstract**

**Background:** Hospital admissions for sickle cell disease (SCD) patients have been poorly characterized. We sought to develop a database to characterize sickle cell disease admissions. We also generated a re-weighted sickle-cell specific Charlson Comorbidity index (S-CCI) that was derived from the Charlson Comorbidity Index (CCI). This addressed the concern that weights for disease-specific populations are often different than those assigned to the general patient population to account...
for interactions between medical conditions.

Methods: We extracted 18,541 visits by sickle cell patients admitted to New York State hospitals between 2005 and 2013 from the SPARCS database. We present data from both a randomly selected derivation cohort, used to develop the S-CCI and a validation cohort.

Results: The S-CCI resulted in small improvements in model fit and discrimination while using fewer covariates, allowing a more parsimonious model. Despite being the most common comorbidity, chronic pulmonary disease was not predictive of mortality. Mortality per hospitalization was 0.61 percent. Many patients (32 percent) were admitted only once during the nine-year period. However, the majority was admitted more frequently with over 15 percent of patients being admitted more than once per year.

Conclusions: A large proportion of hospital admissions were accounted for by a minority of patients. The pattern of comorbidities was notably different than the general population. The S-CCI is a more parsimonious approach to accounting for comorbidities.

JSCDH-D-17-00044: Sickle Cell Disease Transition Assessment and Readiness: Baseline vs. Post- Intervention Analysis

Authors: Caroline Wilder 1, Nisha George 2,4, Hongyan Xu 3, E. Leila Jerome Clay 1,2,4

Affiliation: Augusta University, Augusta GA: 1 Medical College of Georgia, Department of Pediatrics 2 Sickle Cell Center, Georgia Cancer Center, 3 Department of Biostatistics and Epidemiology 4 Department of Medicine, Section of Hematology/Oncology

Abstract

Background: The Transition Program at Augusta University has previously conducted baseline analysis of transition readiness, and determined intervention was necessary to improve medical knowledge and independence. We have focused on expanding our cohort, educating patients and parents, and conducting post-intervention analysis. The purpose of this study is to compare baseline to post-intervention transition readiness of teens and adolescent young adults (AYAs) in our transition program.

Methods: Patients and their parents presenting to routine clinic visits were asked to complete surveys and questionnaires. Patient results were compared to their parents for baseline analysis, and patients and parents were
compared to themselves for post-intervention analysis. We used the TRxANSITION Scale™, STARx self-assessment and HRQoL. Statistical analyses were conducted via Fisher's exact test, and paired t-test at a significance level of 0.05 using R3.3.1.

**Results:** Of the 74 out of 96 patients who participated, 50% were males and 50% females.

59% were teens (age 13-17) and 41% AYAs (18-25). 78% of all participants completed baseline surveys. Of those who completed baseline, 60% received intervention, and 40% were then reassessed. For baseline analysis, The TRxANSITION Scale™ showed parents knew more than their teens about prescribed medications (p=<0.0001-0.0006), proper nutrition (p=0.0203) and contraception (p=0.0015). Responses to 100% of questions about Sickle Cell type, reproductive health, insurance, and transitioning to adult providers showed that parents knew significantly more than their teens (p=<0.0001-0.019; p=<0.0001-0.0013; p=<0.0001; p=<0.0001). The HRQoL assessment showed patients experienced significantly more chest and back pain than their parents realized (p=0.0066; 0.0030). Patients also have more problems than their parents recognize with the way medicine tastes, trouble running, and telling others about having pain and having SCD in general (p=0.0364; p=0.0067; p=0.0038; p=0.0084). Post-intervention analysis using the TRxANSITION Scale™ showed teens significantly improved in knowledge of medications, proper nutrition, and contraception methods. (p=0.0566; p=0.0029; p=0.0215). Teens showed greater independence taking medicine, managing refills, and scheduling appointments (p=0.0091; p=0.029; p=0.0045). It showed that parents' knowledge significantly improved understanding the purpose of medicines, contraception methods, and insurance (p=0.0028; p=0.0269; p=0.0537-0.0548).

**Conclusions:** The larger cohort in this second baseline analysis provided more significant findings than the previous analysis. From this, we were able to more accurately determine the gaps in both patients' and parents' knowledge. The post-intervention analysis showed both patient and parent knowledge improved in several ways. Overall medical independence improved between baseline and post-intervention, likely due to a combination of increased education and maturity.

**JSCDH-D-17-00027:** Acute Care Utilization is more common in patients with sickle cell disease (SCD) who have chronic complications and chronic pain: A Preliminary Report from The ESCAPED Trial

**Authors:** Sophie Lanzkron, MD, MHS
Jane Little, MD Joshua Field, MD Ryan Shows, MD Hang Wang, PhD Rebecca Seufert Jasmine Brooks Brandi Griffin,
Background: We undertook a large multisite observational study collecting prospective data on health care utilization of patients with SCD. No prospective examination of symptom burden has been undertaken in SCD since the Cooperative Study of Sickle Cell Disease. The ESCAPED trial aims to compare patient centered outcomes following management of acute painful vaso-occlusive (VOC) events in the emergency department or in the infusion center. Here, we examine acute care utilization patterns in the first 223 subjects who have completed at least 6 months of follow-up and test determinants of utilization.

Methods: This is an ongoing, prospective cohort study that is recruiting across four sites (Baltimore, Cleveland, Milwaukee, and Baton Rouge). 500 adults with SCD who live in proximity to one of the study sites are being recruited and followed for 18 months. Data from visits for all acute, uncomplicated VOC are collected by chart review and patient interview. We tested for associations between subject characteristics upon enrollment and the number of acute visits during follow-up using Poisson regression.

Results: The average length of follow-up to date is 9.1 months with a range of 6.1-14.2 months. The mean number of acute visits per month for uncomplicated VOC by the cohort was 0.65 (SD 0.87) with a median of 0.35, minimum of 0 and maximum of 5. 43 subjects have had no acute visits. 59% of the cohort are female, the mean age is 35.6 (SD 12.1). 74.3% have sickle cell anemia, 42% are employed and 52% reported having chronic pain. In a multivariate model, factors associated with an independent decrease in likelihood of an acute visit were increasing age, a history of leg ulcers, graduating high school and being employed, while an increase in likelihood of an acute visit was associated with chronic complications (kidney disease, retinopathy, stroke, and avascular necrosis) and chronic pain.

Conclusions: In this cohort, chronic complications are associated with increased acute care visits. The association of chronic pain as an independent risk factor for acute visits, while intuitive, suggests that understanding and managing chronic pain may be central to mitigating pain and decreasing the need for acute care visits in the long term. The prevalence of chronic pain is high in this cohort. The development of therapeutic strategies that address this significant complication of SCD are imperative if we are to both decrease symptom
burden and the need for health care utilization in this population.

*statistically significantly associated with the number of acute visits.

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JSCDH-D-17-00030: Sickle Cell Trait Knowledge and Health Literacy in Caregivers Who Receive in-Person Sickle Cell Trait Education

Keywords: Sickle Cell

Authors: Susan E. Creary, MD, MSc, Ismahan Adan, BA Joseph Stanek, MS, Sarah H. O’Brien, MD, MSc, Deena J. Chisolm, PhD, Tanica Jeffries, MS, LPC, LSW, Kristin Zajo, MA, MS, LGC, Elizabeth Varga, MS, LGC

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Abstract

Background: Sickle cell trait (SCT) affects approximately 8% of African Americans and these individuals are at risk of having children with SCT and sickle cell disease (SCD). Universal newborn screening in the United States detects SCT, but only 16% of individuals of childbearing age with SCT know their status. This is because SCT is not reliably recorded in medical records and SCT may not be consistently or effectively communicated to caregivers. Interventions that increase caregivers' SCT knowledge are important so that individuals with SCT can make informed
decisions about their reproductive health.

Objectives: The objectives of this study were to determine caregivers' baseline health literacy and knowledge about SCT and to determine if in-person SCT education improved caregivers' SCT knowledge and to assess caregivers' satisfaction with their SCT education.

Methods: Nationwide Children's Hospital (NCH) is a SCT referral center in Columbus, OH. At NCH, it is standard that caregivers of infants with SCT who are referred by their primary care providers receive in-person SCT education using visual aids from an educator who has completed a hemoglobinopathy counselor training course. From August 2015-July 2016, we performed a prospective, cross-sectional study of English-speaking caregivers of infants with hemoglobin S-trait who presented for education. Caregivers were excluded if they had SCD or previously received SCT education at NCH. Prior to receiving education, subjects electronically reported their demographic information and completed a health literacy assessment using the Newest Vital Sign (NVS, range 0-6) and an 8-question (true/false, multiple choice) pilot-tested, SCT knowledge assessment (SCTKA) that included items from a published SCT knowledge study and items routinely discussed during NCH SCT education. Lower NVS scores suggest a higher likelihood of limited health literacy. Caregivers with SCTKA scores <75% were considered to have low knowledge. Immediately after receiving education, caregivers repeated the SCTKA and provided feedback about the session. Assessments were not available to the educator during the session. The Wilcoxon Signed-Rank test was used to compare SCTKA scores pre- and post-education. Mann-Whitney tests were used to compare NVS and pre-SCTKA scores between those with high and low SCT knowledge after education.

Results: We recruited 114/124 eligible caregivers who presented during the study period and 113 completed the study. Subjects were mostly female (77%), 18-39 years of age (95.6%), parents or step parents (95.6%) of the child, and some (34.8%) reported that they had SCT. Many caregivers (52.2%) had NVS scores <4, but most (94.7%) reported the education was easy to understand, their questions were answered (99.1%), and they do intend to inform their child of their SCT status (99.1%).

Caregivers' median pre-education SCTKA score significantly improved from 62.5% (IQR=25%) to 87.5% (IQR=12.5%) with education (p<0.0001). Only 38.1% of caregivers had high SCT knowledge pre-education but most (90.3%) achieved high knowledge with education. Caregivers with low SCT knowledge after education had significantly lower NVS scores (median=1, p=0.0286) and baseline SCTKA scores (median=50%, p=0.0032) compared to those with high SCT.
knowledge after education (NVS=3.5, baseline SCTKA median=62.5%).

Discussion: Our study suggests that caregivers’ baseline SCT knowledge is low and improves with in-person education. Despite overall caregiver satisfaction and intensive in-person education from a trained educator, approximately 10% did not achieve high SCT knowledge and our results show that these caregivers may have lower baseline SCT knowledge and health literacy. Assessing caregivers’ health literacy and SCT knowledge prior to education may be useful to allow educators to modify their education to meet the needs of those with limited health literacy and SCT knowledge. Future studies need to determine if tailored education results in high SCT knowledge among all caregivers, if caregivers’ SCT knowledge is sustained, and if high caregiver knowledge results in more individuals with SCT knowing their status and using this knowledge to inform their reproductive decision-making.

JSCDH-D-17-00029: Longitudinal Analysis of the Effectiveness of a Multi-Disciplinary Inpatient Program for the Management of Pediatric Sickle Cell Pain Crises

Authors: Lyn Balsamo PhD¹, Veronika Shabanova, MPH, MS², Donna-Ann Thomas MD¹, Farzana Pashankar MD¹

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Abstract

Background: Pain is the most common reason for hospitalization among patients with sickle cell disease (SCD). We implemented a multidisciplinary program aimed to reduce admissions and length of stay (LOS). Five components were developed and implemented: 1)EPIC SCD order set; 2)PCA order set with weaning paradigm; 3)Psychosocial support/education groups; 4)Daytime schedule; 5)Discharge planning with home pain management teaching and Pain Action Plan.

Method: This longitudinal study followed 232 pediatric patients with SCD, a subset of whom were admitted to Yale-New Haven Children's Hospital for vasocclusive crisis between September 2011 (12 months before program initiation (TO)) and 2015 (3 years after program implementation (T1, T2, T3)). Patient characteristics, admissions, hospital days, and LOS were abstracted from medical records and summarized. Univariate and multivariate Poisson regressions were used to determine factors associated with number of admissions, LOS, and high admissions (≥4/year).

Results: Table 1 describes characteristics of patients admitted. There was a decrease in hospital days
between T0 and T3 (p<0.001) and number of admissions between T1 and T3 (p=0.005). In adjusted analyses, age (OR=1.1, p< 0.001) was associated with yearly admissions. Patients with mental health (MH) diagnosis (OR=3.4, p=0.031) or living in two-parent households (OR=2.8, p=0.030) had longer LOS. A small subset had >4 admissions/year, accounting for 39 to 64% of total admissions and at least 48% of hospital days. Age (OR=1.471, p=0.019), MH diagnosis (OR=66.588, p=0.001), and hydroxyurea use (OR=6.232, p=0.002) were associated with >4 admissions/year. Over time, those with a MH diagnosis were less likely to have >4 admissions/year (OR=0.364, p=0.019).

Conclusions: A multidisciplinary program implemented over 3 years reduced total hospital days and number of admissions by 40 and 22% respectively. Older age and MH diagnosis were associated with >4 admissions/year. Over time, those with MH history were less likely to have high admissions. This group particularly benefited from milieu structure, psychosocial interventions, and clearer pain management strategies.

Table 1. Patient characteristics and admissions over time

<table>
<thead>
<tr>
<th></th>
<th>T0</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients admitted/Patients with &gt;4 admissions</td>
<td>53/13</td>
<td>50/13</td>
<td>53/8</td>
<td>45/9</td>
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<tr>
<td>Mean age at admission, years (SD)</td>
<td>11.8 (5.7)</td>
<td>13.1 (5.2)</td>
<td>11.9 (5.5)</td>
<td>11.4 (5.1)</td>
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<tr>
<td>Gender (Male/Female)</td>
<td>27/26</td>
<td>27/23</td>
<td>29/24</td>
<td>26/19</td>
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<tr>
<td>Genotype (SS/SC/Sβ0/Sβ+)</td>
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<td>39/6/4/1</td>
<td>39/8/4/2</td>
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<td>17/33</td>
<td>20/33</td>
<td>16/29</td>
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<td>Number of admissions/Total hospital days</td>
<td>143/684</td>
<td>158/727</td>
<td>120/577</td>
<td>112/413.5</td>
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<tr>
<td>Mean length of stay, days (SD)</td>
<td>4.78 (4.08)</td>
<td>4.63 (3.09)</td>
<td>4.85 (3.66)</td>
<td>3.69 (2.12)</td>
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HEALTH SERVICES RESEARCH

JSCDH-D-17-00042: Our Hands, Our Health! A Promising Group Healthcare Model for Sickle Cell Disease and Readiness for Transition

Authors: Crystal L. Patil, PhD, Angela Rivers, MD, PhD, Brigid Packer, BSN, APN, Ronisha Edwards, BA, Brooklyn Hastings, Divya Bhandar,
Affiliation: University of Illinois at Chicago College of Nursing

Abstract

Background: The transition of adolescents and emerging adults (AEAs) from pediatric to adult care is challenging; this is especially true for those with sickle cell disease (SCD) because transition coincides with a time period of rapidly increasing risk for mortality. To address the unique transition needs of those with SCD, our team developed and piloted an innovative group healthcare model based on a well-established model, Centering® Healthcare. This model puts the patient and their healthcare experiences at the center of care. Centering is shown to be highly satisfying to both patients and providers, and is expanding rapidly in the US and internationally. Centering's combination of evidence-based effectiveness and its well-defined, replicable core components make this model an attractive one to adapt. Our first aim was to adapt and develop a centering-based group healthcare model for SCD transition. Our second aim was to conduct a feasibility study so that we could revise the program for use in a full-scale pilot.

Methods: Using constant comparative techniques, we reviewed the core components of the Centering model and systematically integrated these as we produced the Our Hands, Our Health! group healthcare model. Through direct observation and health provider interviews, we documented current practice and produced an implementation strategy. Last, with four female participants, we conducted a feasibility study. We pretested all content and documented fidelity to the core components of the Centering model. We used direct observation and semi-structured qualitative interviews with participants to assess acceptability and feasibility.

Results: We produced the Our Hands, Our Health! program and associated Facilitator’s Guide. We present comparative tables to show that the core features of the Centering Model were retained. We describe implementation procedures including integration in the clinic. All four participants stated that they preferred group care to individual care. Participants also described the value of shared experiences, appreciation for the learning environment, and assessed their readiness for transition. This feasibility study showed that Our Hands, Our Health! is an acceptable and feasible model for AEAs with SCD. In response to lessons learned, we modified materials, increased the number of sessions from 6 to 10, and adjusted the program schedule.

Conclusions: The Our Hands, Our Health! program is a promising patient-centered model for healthcare delivery during transition. The next step is to finalize the materials revisions and conduct a pilot of Our Hands, Our Health! so that we will be ready to conduct an effectiveness study.
JSCDH-D-17-00037: Caregiver perspectives on family psychosocial risk and adaptive coping strategies in pediatric Sickle Cell Disease: informing the adaptation of the Psychosocial Assessment Tool (PAT)

Authors: Steven K. Reader, Ph.D., Nicole M. Ruppe, B.S., Janet A. Deatrick, Ph.D., Diana Rash-Ellis, M.S.W., Jean R. Wadman, M.S.N., C.P.N.P., Robin E. Miller, M.D., Anne E. Kazak, Ph.D., ABPP

Affiliation: Nemours Children’s Health System, Wilmington, Delaware (Reader, Ruppe, Rash-Ellis, Wadman, Miller, Kazak); University of Pennsylvania School of Nursing, Philadelphia, Pennsylvania (Deatrick)

Abstract

Background: Families of children with Sickle Cell Disease (SCD) face significant illness and life-related psychosocial adversity that can affect health outcomes. There is currently a lack of validated and culturally-specific psychosocial screening measures for families of children with SCD. This study is an independent part of a larger project assessing the acceptability and utility of the Psychosocial Assessment Tool (PAT) as a screener of family psychosocial risk in pediatric SCD. The purpose of this study was to explore the lived experience of families coping with SCD in terms of family psychosocial challenges and adaptive coping strategies, to help inform the adaptation of the PAT for this population.

Methods: Caregivers (n = 22) of youth with SCD receiving care through the Hematology clinic at a pediatric academic medical center completed the PAT and a semi-structured qualitative interview. Constant comparative analyses involved coding interviews, organizing coding categories into themes, and systematically reintegrating themes into a conceptualization that reflected the experiences of caregivers. Feedback from caregivers was used to generate pilot test items for the PAT.

Results: Caregivers focused on salient family stressors including financial/employment concerns, illness-related caregiver stress and anxiety, and school issues. Caregivers identified a number of adaptive coping strategies including social support from family, community, and the hospital team, relying on religion and faith, and using positive engagement strategies (positive mindset, participation in valued activities). Caregivers noted that the PAT can serve to increase awareness of psychosocial concerns and facilitate dialogue within families and between families and the healthcare team. Caregivers were predominantly female, and no notable differences were found in the qualitative analyses based on caregiver or patient gender. Based on caregiver feedback, pilot test items were generated for the PAT to assess...
school absences, religious coping, and family mobility.

**Conclusions:** Families of youth with SCD face significant illness- and life-related psychosocial stressors but demonstrate resiliency in using a number of adaptive coping strategies. Study results support the continuing development of the PAT as a family psychosocial risk screener in pediatric SCD that can enhance the delivery of evidence-based care and reduce health disparities.

**JSCDH-D-17-00011: Vitamin A Supplementation Associated with Improved RBC Indices and Fetal Hemoglobin in Subjects with Hgb SS Disease**

**Authors:** J. Brownell, J. Schall, C. McAnlis, K. Smith-Whitley, C. Norris, V. Stallings

**Affiliation:** Children’s Hospital of Philadelphia Philadelphia, Pennsylvania UNITED STATES

**Abstract**

**Background:** Previous studies have shown that suboptimal Vitamin A status is prevalent in children with type SS sickle cell disease and was associated with hospitalizations, poor growth, and poor hematological status. The etiology of suboptimal Vitamin A status in SCD is unknown, but may be due to an increased requirement related to the chronic inflammatory state, low dietary intake, and/or excess loss in stool or urine. Current clinical treatment includes little nutritional care other than folic acid. Vitamin A supplementation, if effective, may prove to be a low-cost, feasible adjunct treatment of complications in this population.

**Methods:** As part of a larger study to investigate the optimal dose for daily oral Vitamin A in subjects with type SS sickle cell disease, hematological data were collected on 22 subjects between the ages of 9 and 20 years of age at baseline and after supplementation with either 3000IU or 6000IU of Vitamin A daily for eight weeks.

**Results:** One subject was lost to follow up. Of the remaining 21, 16 were on hydroxyurea at the initiation of the study. No subjects underwent any medication changes. Fetal hemoglobin increased from a mean 16.4 g/dL pre-supplementation to 18.8 g/dL post-supplementation (p=0.02). Fetal hemoglobin increased regardless of whether subjects were taking hydroxyurea; however, the effect was only significant in the hydroxyurea group. Mean erythrocyte indices showed a statistically significant improvement; mean cell volume increased from 87.0 fl to 89.8 fl
(p=0.01), while mean cell hemoglobin increased from 30.7 pg to 32.0 pg (p=0.006). Concurrently, serum aspartate aminotransferase decreased from 53 U/L to 45 U/L (p=0.01). Notably, these effects were only seen in subjects taking hydroxyurea. Alkaline phosphatase decreased from 151 to 138 (p=0.03). Mean hemoglobin and hematocrit did not change. None of the changes were associated with dose of Vitamin A.

Conclusions: Overall, these data suggest a positive, clinically meaningful response to Vitamin A supplementation, particularly in subjects already on hydroxyurea. Indices of erythrocyte health are overall increased, along with a concurrent decrease in two markers of hemolysis. Though there was no change in hemoglobin, there was a significant increase in fetal hemoglobin. Fetal hemoglobin inhibits aggregation of hemoglobin S in erythrocytes, reducing episodes of vaso-occlusive crises. The role of vitamin A as an effective, low-cost adjunct to current therapy for SCD merits further investigation.

JSCDH-D-17-00031: Patients with sickle cell disease who use illegal drugs have increased frequency of vaso-occlusive crises that required hospital admission

Author: Samir K. Ballas MD
Affiliation: Cardeza Foundation for Hematologic Research, Thomas Jefferson University, Philadelphia, PA

Abstract

Background: Treatment of the recurrent sickle cell crisis is mostly opioids in combination with NSAIDS and adjuvants. Patients may resort to the use of illegal drugs to achieve better pain relief than prescription analgesics. The objective of this study was to determine if patients with SCD using illegal drugs had decreased frequency of crises that required treatment in the Emergency Department and/or hospital than patients who did not.

Methods: This was a retrospective study in which 307 random urine drug screen tests were done on 76 patients (40 males and 36 females). Urine samples were analyzed for the presence of amphetamine, benzodiazepines, opiates, barbiturate, cannabinoid, methadone and phencyclidine. Samples were classified as either positive or negative for each drug.

Results: All urine drug tests were positive for the prescribed opioids and all were negative for amphetamine. Thirty-nine of the 76 patients tested positive for illegal drugs and 37
patients tested negative. The number of patients tested positive for each illegal drug varied between 4 for phencyclidine and 37 for cannabinoid. There was no significant difference in the ages of males and females whether they used illegal drugs or not (32.5 ± 8.2 v 34.1 ± 7.4). However, males who used illegal drugs were significantly younger (p < 0.001) than males who did not (31.6 ± 8.0 v 36.3 ± 8.0). Surprisingly, the most important aspect of the study was the effect of illegal drug use on the frequency of utilization of medical facilities. Patients in the positive cohort had crises that required hospital admission more frequently than the negative group: 2443 v 1602 respectively (p < 0.05). In addition, clinic visits were significantly greater for the users of illegal drugs: 1325 v 1138 respectively (p < 0.05). Crises that were treated in the ED without hospital admission were similar for both groups (p > 0.05). The illegal drug most commonly used was cannabinoid.

**Conclusion:** Together these data suggest that patients using illegal drugs, mostly marijuana, were more often in severe pain that required treatment in medical facilities than non-users. This difference could be due to the quality of the drugs used, the neuronal effects of the drugs and the severity of pain in the users of drugs. The role of marijuana in the treatment of sickle cell pain seems more complex than previously thought. Further controlled trials are needed to clarify this issue.

**JSCDH-D-17-00045:** Vitamin D deficiency in sickle cell disease: The role in the incidence of vaso-occlusive crisis, hospitalization rates and length of stay.

**Authors:** Deepak Choudhary, Sara Zarzoso-Fernandez, Sandy Lee, Levon Agdere, Jolanta Kulpa, Yang Liu and Revathy Sundaram

**Affiliation:** New York Methodist Hospital Brooklyn, NY, UNITED STATES

**Abstract**

**Background:** Sickle cell disease (SCD) is a common and severe genetic disorder. The bones of children with SCD are affected by infarcts, osteoporosis, osteomyelitis or avascular necrosis. Low levels of vitamin D could further impact the bone health of patients with SCD. Vitamin D deficiency (VDD) is one of the most common nutritional conditions in SCD due to decreased appetite, inability to absorb nutrients and increased basal metabolic rate. Several studies have documented low vitamin D levels in children with SCD. Children with SCD have 5.3-fold increased risk of developing VDD
compared to healthy African-American controls. Vitamin D has immunomodulatory and antimicrobial properties that may provide beneficial effects for prevention of vaso-occlusive crisis (VOC).

**Methods:** The study was conducted in a community teaching hospital in Brooklyn. A retrospective chart review (n=90) was conducted for episodes of VOC in the three years preceding the collection of Vitamin D levels. Vitamin D deficiency (VDD) was defined as less than 20 ng/ml. A sickle cell template was created in the electronic medical record system. Data regarding emergency room (ER) visits, number of admissions and length of stay was analyzed and associated with vitamin D levels.

**Results:** When vitamin D levels were <10 ng/ml, patients were more likely to have at least one ER visit (p=0.014), at least one admission (p=0.013) and longer length of stay (p=0.003). When vitamin D <15 ng/ml, patients were more likely to have more admissions (p=0.04) and a longer length of stay (p=0.03) as well. Patients with vitamin D levels of 15-20ng/ml were not found to be statistically significant.

**Conclusion:** There was a statistically significant association between very low levels of Vitamin D and rates of ER visits, admissions and length of stay. This study offers us opportunities to initiate therapeutic interventions to correct VDD and study the impact of VDD on the morbidity of sickle cell disease.

**JSCDH-D-17-00003:** ASSESSEMENT of HEMATOLOGICAL DATA in a COHORT of EUROPEAN CHILDREN WITH SICKLE CELL DISEASE (SCD) TREATED WITH HYDROXYUREA (HU): CAN TODAY EUROPEAN CENTERS APPLY THE LESSONS FROM the TWiTCH STUDY?"

**Abstract**

**Background:** In the TWiTCH trial, children in the HU arm received the drug at the maximum tolerated dose (MTD) with escalation of dosage until absolute neutrophil count (ANC) is <3.0 x10⁹/L. Median HU MTD was 27.4 mg/kg/day. Final average HbF% and ANC were 24.4% and 3.6 x10⁹/L.
respectively. Most European centers do not try to reach the MTD.

Our study aimed to determine median HbF% and ANC in the children included in the European ESCORT-HU cohort, a non-interventional, prospective, observational open-label study on the efficacy and safety of HU titrated dose formulations for SCD (Siklos®) in order to see whether they were within the ranges demonstrated to exert brain protection in the TWiTCH trial.

Methods: In ESCORT-HU out of the global cohort of 992 patients, 386 patients were aged 2 to 18 years at the time of study initiation. Among them, 233 patients were HU treatment-naïve and initiated Siklos® treatment. A follow-up of at least 12 months and data allowing biological or clinical efficacy evaluations were available in a subgroup of 139 not previously treated with HU patients. In the global cohort, 31 children were treated for cerebral vasculopathies.

Results: After 12 months of treatment in the subgroup of children not previously treated with HU, the mean used dose was 20.73± 6.42 mg/kg/day. The variations of HbF% (+ 8.01% ± 8.38%) and ANC (-73.23 ± 641.43 10⁹/L) were respectively p<0.001 and p<0.05. 48.83% of the patients has reached ANC <3.0 x10⁹/L and mean final Hbf % and ANC were 15.04 ± 0.95 % and 4.90 ± 3.25 x 10⁹/L.

Regarding efficacy items for the same subgroup, the % of patients having had at least 1 painful episode, or at least 1 acute chest syndrome, or at least 1 hospitalization or at least 1 blood transfusion after 12 months under HU decreased significantly (respectively -38.6%, -75.8%, -44.6%, -49.9%; p<0.001 for all).

Conclusion: We show that children included in the ESCORT cohort received median HU dosage quite lower than the one given to children included in the TWiTCH trial which resulted in quite lower HbF%. Nevertheless, this dosage was sufficient to very dramatically reduce SCD-related events. Whether it can exert the same brain protection as the one demonstrated in the TWiTCH study is so far not known. We encourage physicians to reach MTD when the indication for HU is brain protection.

BASIC SCIENCE

JSCDH-D-17-00007: SANGUINATE Returns RBCs To More Normal Morphology in Patients With VOC
Authors: Gershwin Blyden, Lanetta Bronte, *Peter Buontempo, Cathy Buontempo, Ronald Jubin, and Abraham Abuchowski

Affiliation: *Prolong Pharmaceuticals South Plainfield, New Jersey UNITED STATES

Abstract

Introduction: Vaso-occlusive crisis (VOC) is the physiological consequence of morphological changes in red blood cells (RBCs) within the microvasculature. A wide variety of factors can influence a VOC, but all events have the underlying molecular characteristics of low oxygen in RBCs promoting hemoglobin polymerization. The loss of RBC circularity prevents the hypoxic cells from effectively flowing through the microvasculature that further expands hypoxia to tissues at sites distal to blockade. Current treatment regimens that reduce absolute blood HbS levels (transfusion and hydroxyurea) have demonstrated complete elimination is not necessary to promote a positive clinical effect. SANGUINATE is a dual gas transfer agent that has been shown to revert SCD RBCs to a more normal morphology in vitro. A phase 2 study is underway to determine whether infusing SANGUINATE during an acute VOC episode can reduce the need for IV opiates and prevent hospitalization. Blood samples were collected to ascertain the impact of SANGUINATE upon RBC morphology.

Methods: Whole blood samples were collected prior to infusion, at the time of patient discharge and 72 hours post-infusion. Samples were shipped by priority overnight to Prolong Pharmaceuticals for imaging cytometry and shape analysis.

Results: SANGUINATE infusion caused a shift in the number of abnormally shaped cells to a more normal morphology, which is consistent with in vitro results. This shift occurred within hours of infusion and was sustained at the 72-hour sampling period. The placebo treated patient showed no shift in cell morphology during the sampling period.

Conclusion: SANGUINATE returns RBCs to a more normal shape in patients experiencing VOC and for a prolonged period. These results support the use of SANGUINATE in this patient population to reduce opiate use and prevent hospitalization for VOC.

JSCDH-D-17-00026: Anti-sickling Properties of a Novel Structurally-Enhanced Pyridyl Derivatives of Vanillin
Authors: Martin K Safo, PhD Piyusha P Pagare Mohini Ghatge, PhD Guoyan Xu, PhD Ronni P Safo Aheema Gazi Qiukan Chen Carla Casu, PhD Tanya David, PhD Jurgen Venitz, MD PhD Yan Zhang, PhD Osheiza Abdulmalik, DVM

Affiliations: The Children's Hospital of Philadelphia Philadelphia, PA UNITED STATES

Abstract

Candidate drugs to counter intracellular polymerization of deoxygenated sickle hemoglobin (Hb S) continue to represent a promising approach to mitigating the primary cause of the pathophysiology associated with sickle cell disease (SCD). As part of our efforts to develop novel efficacious drugs with sustained duration of action, we modified our previously reported pyridyl derivatives of vanillin by incorporating an ester group on the pyridine moiety, and designated this class of compounds as PP-series. The alterations are anticipated to confer specific properties: increase binding interactions with the protein and thus the stability of the modified, high-affinity Hb (Schiff-base adduct); as well as perturb surface-located F-helix of deoxy-Hb S, and therefore stereospecifically destabilize polymer contacts. The modifications are also expected to protect the active aldehyde moiety of the drug from extensive and rapid enzymatic metabolism into the inactive alcohol and/or acid analogs.

First, we investigated the in vitro pharmacokinetic/pharmacodynamic (PK/PD) properties of the PP compounds in normal blood to ascertain sustained binding and modification of human Hb. To establish the mode of interaction with Hb, we conducted x-ray crystallographic studies with representative compounds. Subsequently, we conducted in vitro screening assays with blood from individual donors with homozygous SS to test for inhibition of sickling, modification of Hb to the high-affinity (adduct) form, as well as for a direct left-shift in oxygen equilibrium curves (OEC).

To test the degree and duration of Hb modification, we incubated 0.5, 1, and 2 mM concentrations of the PP compounds: PP2, PP3, PP4, PP6, PP8, PP9 and PP1; with normal adult blood (hematocrit: 30%) at 37°C for 24 h. At defined time points, aliquot samples were obtained, fixed, and analyzed by cation-exchange HPLC. Hb modification (for all three doses) were sustained for the entire 24 h experimental period, compared to adduct formed by INN310, the precursor compound, which declined after 8 h. These findings suggested that our modifications appear to successfully limit drug metabolism in red blood cells. Next, we tested the anti-sickling properties of the four most promising candidates in vitro by incubating 0.5, 1, and 2 mM concentrations with blood from subjects with homozygous SS (hematocrit: 20%), under hypoxic conditions (4% O2/96% N2) at 37°C for 2 h, and assessed sickling by microscopy. Successively, we conducted cation-exchange HPLC analyses to measure the degree of Hb modification, and O2 equilibrium curves (OEC) to assess p50 shifts. The compounds showed a dose-dependent inhibition of cell sickling, Hb modification (adduct), and corresponding changes in Hb oxygen affinity (Δp50, %). All four compounds showed complete inhibition of sickling at 2 mM concentrations, while PP6...
and PP11 had the most profound $\Delta p50$ values precursor.
($\sim 65\%$ and $55\%$ at 2 mM, Table 1).

Summarily, our results establish PP-While the PP compounds, similar to the parent compounds as a novel, promising group of compound, bind symmetrically at the $\alpha$-cleft to topotent anti-sickling agents. We have form Schiff-base adducts with the N-terminal successfully improved in vitro PK/PD Val1 amines of Hb, several important binding properties, while detailed in vivo PK/PD studies differences that include interactions with the F-helix and overall enhanced interactions with the Hb illuminate the observed biochemical differences among the compounds and the

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<tr>
<th>Drug</th>
<th>Conc (mM)</th>
<th>Modified Hb (%)</th>
<th>$\Delta p50$ (%)</th>
<th>Sickling Inhibition (%)</th>
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Table 1
Establishment of Steady State Adhesion Indices in Sickle Cell disease: Clinical Application of a Standardized Adhesion Bioassay

Authors: Jennell White, PhD Ke Liu, PhD Xiufeng Gao, MD Timothy A. Thornton, PhD Ahmar Zaidi, MD Michael U. Callaghan, MD Patrick C. Hines, MD/PhD

Affiliation: Wayne State University DETROIT, UNITED STATES

Abstract

Individuals with Sickle cell disease (SCD) have erythrocytes that are more adhesive than erythrocytes from unaffected individuals. An association between sickle erythrocyte adhesion to vascular cell adhesion molecule (VCAM-1) and disease severity has been previously shown. A variety of laboratory-based adhesion assays have been used to study anti-adhesive therapies in SCD. We have established pulsatile flow as a key element to measuring pathologically significant adhesive interactions, and have established a standardized platform to measure clinical adhesion indices that incorporates pulsatile flow. This report evaluates the utility of a standardized, microfluidic flow-based adhesion assay to establish clinical adhesion parameters at steady state. Blood samples were collected in sodium citrate from SCD subjects at steady state (average 25.9yrs, range 13-48 years). In this assay, 30 microliters of whole blood was flowed over immobilized VCAM-1 at standard physiologic flow conditions (1 dyne/cm², 1.67Hz). An adhesion index was established by quantifying erythrocytes adhering within a standard viewing area (cells/mm²), and could be obtained within 6-9 min. Steady state adhesion varied from sample-to-sample (n=169; mean = 365.9 ± 248.9; median = 297 cells/mm²). A linear mixed model analysis was conducted to assess associations with steady state adhesion measurements. Steady state adhesion was positively correlated and significantly associated with C-reactive protein (CRP; r=0.212; p=0.0297) and reticulocyte percent (r=0.331; p<0.0001), and negatively correlated and significantly associated with hematocrit (r=-0.182; p=0.0014) and fetal hemoglobin (r=-0.429; p=0.0045). This microfluidic flow adhesion assay was developed to obtain standardized adhesion indices from SCD blood samples, and has been previously utilized to assess the effect of a broad range of SCD modifying drugs on adhesion. Our data confirm the previously established association between adhesion and inflammation (CRP). The positive relationship between reticulocyte percentage and adhesion reflects a greater expression of VLA-4 on reticulocytes and immature erythrocytes, which has been previously described. The negative relationship between hemoglobin and adhesion suggests a larger proportion of highly adhesive immature erythrocytes. Fetal hemoglobin has been associated with reduced disease severity, likely
explaining the negative correlation with adhesion. This study establishes steady state adhesion indices with a standardized assay available for investigators and clinicians to monitor adhesion indices, explore the clinical implications of abnormal adhesion indices, and objectively assess the adhesive response of SCD modifying therapies.

**JSCDH-D-17-00033: Increased Expression of Cellular Stress Protein, α-SYNUCLEIN(SNCA) within Normoxic and Hypoxic Brains of SCD Mice: Implications for Neurocognitive Dysfunction in Sickle Cell Disease Patients**

**Authors:** Fitz Tavernier B.S', Kori Bradley, B.S', Amrita Pawar B.S', Grace Fu B.S', Ama Achampong B.S', Jennifer Addo B.S', Mariam Hamid B.S', Amanda Sankar, MD', Rebekah Urbonya B.S', Andrea Mathias, B.S', Aaran Varatharajan B.S', Kwaku Osei Bonsu, B.S', **Andrew Campbell, MD**

**Affiliation:** 'Pediatric Hematology/Oncology, University of Michigan, Ann Arbor

**Abstract**

**Background:** The aggregation of the protein α-synuclein (SNCA) is linked to neurocognitive dysfunction in Parkinson’s disease and Alzheimer’s Disease. Alpha synuclein aggregate into Lewy bodies, which are prevalent in patients with Parkinson’s disease. Neurocognitive dysfunction is also prevalent within sickle-cell disease (SCD) patients. Strokes, silent and overt, are also well known complications within SCD resulting in neurocognitive deficits; however, it is not found within all SCD patients with neurocognitive dysfunctions. SNCA has been found to be elevated in reticulocytes and pro-inflammatory states and peripheral blood mononuclear cells of hypoxic SCD patients (Nakai et al 2007, Zhang et al 2014). Since SCD patients have high reticulocyte counts and are in an chronic pro-inflammatory state, we investigated SNCA expression within the Brains of our Wild type and SCD mice under normoxic conditions and hypoxic conditions that would represent an acute pro-inflammatory state, which has been implicated in producing SNCA aggregates.

**Materials & Methods:** SNCA qRT-PCR mRNA expression within Brains of Normoxic Wild type(WT) Control Mice (n = 5, Mean Age=5.5m/o) was compared to expression within the Brains of Normoxic SCD mice (n=5 Mean Age 5.7 m/o). Additionally, in a separate experiment, Brain SNCA expression of Normoxic SCD Mice (N=4, Mean 5.1m/o) controls was compared to sickle-cell mice, under hypoxic conditions (n = 4, Mean 5.5 m/o). To simulate hypoxic conditions mice were placed in a chamber for 8 hours that was infused with nitrogen to lower the oxygen levels to FiO2 of 7%. The cDNA from normoxic and hypoxic mice brains were synthesized and then subject to Quantitative Real Time Polymerase
Chain Reaction (qRT PCR) to determine the expression level of SNCA in Normoxic WT mice, Normoxic SCD mice, and Hypoxic SCD mice. The fold expression of SNCA was normalized in triplicates was compared to expression of GAPDH, a housekeeping gene. The cDNA samples for each mouse were done in triplicates and the relative expressions of the three samples were averaged.

Results: SNCA expression were significantly higher in the Brains of Normoxic SCD mice (mean 9.95, sd 3.06) compared to Normoxic WT Control mice (mean 5.04, sd 1.09) p= 0.01. Further, SNCA Brain expression was significantly higher within the SCD Normoxic Brain (8.75) vs the SCD Hypoxic Brain (15.25).

Conclusion: There are significant differences of SNCA expression between the brains of wildtype mice and sickle-cell mice. Sickle-cell mice have a higher expression of SNCA in the brain, even more so when subject to hypoxic conditions. SCD complications and associated comorbidities that result in acute and chronic hypoxia could lead to an increased expression of SNCA in the brain, possibly contributing to neurocognitive dysfunction seen in non-stroke patients.

JSCDH-D-17-00047: Inhibition of LSD1 improve RBC survival by reducing mitochondrial retention and associated ROS levels in the red blood cells of a mouse model of sickle cell disease

Authors Ramasamy Jagadeeswaran, Ph.D. Maria Armila Ruiz, BA Vinzon Ibanez, BS Joseph DeSimone, Ph.D. Donald Lavelle, Ph.D. Angela Rivers, M.D.,Ph.D.

Affiliation: University of Illinois, Chicago Chicago, IL UNITED STATES

Background: Sickle cell disease (SCD) is an inherited blood disorder that affects millions of people worldwide. Individuals with SCD suffer from HbS polymerization which leads to chronic hemolytic anemia, painful crises, multisystem organ damage, and a shorter lifespan. Elevated levels of fetal hemoglobin (HbF) are known to decrease HbS polymerization and associated with less disease severity and increased lifespan. In addition to HbS polymerization there is an excessive formation of intracellular reactive oxygen species (ROS) in SCD red blood cells which accelerates their hemolysis. We have recently shown that RN-1, a lysine specific demethylase-1 (LSD-1) inhibitor, induces high levels of HbF in the baboon while in a SCD mouse model, HbF levels did not exceed 3%, a level too low to achieve clinical benefits. Despite the low levels of HbF induced by RN-1 in SCD mice, a reduction in disease pathology was observed accompanied by an increased RBC lifespan suggesting that RN-1 may reverse disease pathology by a novel mechanism independent of HbF induction. The observation that RN-1 treatment of SCD induced PGC-1α, a
transcription factor involved in both mitochondrial biogenesis and clearance suggested the hypothesis that mitochondrial clearance was impaired in SCD mice, contributing to the formation of excessive reactive oxygen species and thus accelerating the disease process.

Methods: To test this hypothesis, we examined the percentage of RBC retained mitochondria in peripheral blood of SCD mice compared to control AA mice and effect of RN-1, and Sirolimus in SCD mice by Flowcytometry and confocal microscopic analysis using TMRM, APC-conjugated CD71 antibody and CM-H2DCFDA.

Results: We observed that a significant proportion of RBCs in SCD mice abnormally retain mitochondria compared to normal control mice. [Control: 0.29% ± 0.18%; SCD: 16.68%± 1.9%, p<0.0001]. Treatment with RN-1 reduced the abnormal number of RBCs with mitochondria (4.96+1.0%, p<0.0005). In addition, a decrease in the fraction of RBCs retaining mitochondria (6.4+1.8%, p<0.002) was also observed in SCD mice treated with the mTOR inhibitor Sirolimus, a known inducer of mitophagy. Increased RBC survival (>60%) and a reduction of ROS in mature RBCs coupled with a decreased mitochondria retaining RBC fraction after in vivo treatment with either RN-1 or Sirolimus was observed.

Conclusion: Based on this data, mitophagy-inducing drugs have the potential to be developed as a novel therapeutic approach for the treatment of SCD patients. Our findings suggest that the LSD-1 inhibitor RN-1 improves sickle cell RBC survival by eliminating intracellular ROS accumulation. Therefore, LSD-1 inhibitors may have a dual therapeutic benefit in SCD through epigenetic modulation to increase HbF and reduce ROS by increasing mitochondrial clearance.

JSCDH-D-17-00004: Effects of Transfusions and Hydroxyurea on Pulmonary Functions Tests in Children with Sickle Cell Anemia

Authors: Nnenna Ukachi, MD Elizabeth Fiorino, MD Meredith Akerman, MS Abena Appiah Kubi, MD Maria Teresa Santiago, MD Banu Aygun, MD

Affiliation: Steven and Alexandra Cohen Children's Medical Center New Hyde Park, NY UNITED STATES

Abstract

Background Children with sickle cell anemia (SCA) can have obstructive and restrictive patterns on pulmonary function testing (PFT). However, the effects of disease modifying treatments on these test results are not known. We sought to describe the evolution of PFT results in our SCA patients, and analyze whether transfusion therapy or hydroxyurea had any beneficial effects on results over time.

Objectives To compare at least 3 consecutive PFT results of patients with SCA on transfusion therapy or hydroxyurea with those on no therapy.
Methods: We performed a retrospective chart review of patients between 11 and 21 years who had undergone three or more consecutive PFTs at least one year apart. We compared FEV1, FVC, FEV/FVC, and FEF25-75 of patients who were on treatment with transfusions or hydroxyurea for at least 4 years with those not on treatment (controls). We analyzed each PFT outcome using repeated measures analysis of variance (RMANOVA) models with a mixed model approach to assess trends over time.

Results: We reviewed 15 charts; 6 patients were on hydroxyurea, 3 were on transfusion therapy and 6 were controls. Cohorts shared similar demographic characteristics such as ethnicity, age at first PFT (10.1 vs 9.6 vs 10.3) and gender. Median intervals between PFTs were 23 – 29 months for T1-T2 and 16 - 32 months for T2-T3. Additionally, 50% of patients in each respective cohort had a 4th PFT at T4 with median interval of 12 – 25 months. We observed normal percent predicted values in transfusion cohort for all PFT measures from T1 through T4. Our hydroxyurea and control cohorts had low baseline percent predicted FEV1 (70.5 vs 72.8) and FEF25-75 (59.7 vs 63.3) at T1. Improvements in FEV1 (93.8 vs 75.7, p = 0.50) and FEF25-75 (78.3 vs 64.4, p = 0.86) were noted in the hydroxyurea cohort by T3 and T4 when compared to control cohort.

Conclusion: Our preliminary findings suggest that pulmonary function is preserved in children with SCA on transfusion therapy. Those on hydroxyurea showed improvement in FEV1 and FEF25-75% over several years, suggesting that hydroxyurea may have a mitigating effect on the obstructive lung disease in this patient population. Although we could not determine statistical significance given our sample size, further exploration of this association is warranted.

BREAKOUT SESSION II- SUNDAY, APRIL 30, 2017

CLINICAL EPIDEMIOLOGY

JSCDH-D-17-00046: The Effects of Single Music Therapy Session on the Pain of Adult Patients with Sickle Cell Disease: Results of Mixed Methods Study

Authors: Samuel Rodgers-Melnick, MT-BC ¹, Coretta Jenerette, PhD, RN, CNE ², Nadine Matthie, PhD, RN, CNL ³, Pingfu Fu, PhD ⁴, Seunghee Margevicius, DNP, MA, RN ⁴, Tara Pell, MA, MT-BC ¹, Deforia Lane, PhD, MT-BC ¹, Jane Little, MD ⁵

Affiliation: ¹University Hospitals Seidman Cancer Center, Cleveland, OH; ²University of North Carolina at Chapel
Abstract

Background: Individuals with sickle cell disease (SCD) may benefit from adjunctive nonpharmacologic strategies to manage pain—the hallmark of the disease. Music therapy (MT) has been effective in managing pain in oncology and palliative care but has not been investigated in SCD. Here, we studied the impact of a single MT intervention on the pain of adults with SCD as an adjunct to conventional treatment during a vaso-occlusive crisis.

Methods: This study utilized a mixed methods intervention design. Sixty adults with SCD were recruited from an outpatient clinic. At their next visit to an infusion center for same-day pain treatment, participants were randomized to one of three 20-min sessions: 1) a session with a music therapist (MT), 2) listening to patient-selected music on an iPod (ML), or 3) standard care without music (Control). Visual analog scales of pain intensity (VASPI), pain relief (VASPR), and mood (VASMOOD) were assessed pre- and post-intervention by a researcher blinded to randomization. Following the intervention, a random selection of patients from the MT or ML groups was interviewed to determine the acceptability and feasibility of the music interventions. Multiple logistic regression analysis was conducted with VAS scores split into two categories using median changes at cutoff points to create binary outcome variables. Treatment effects were adjusted for age, gender, and pre-intervention VAS scores.

Results: Twenty patients were randomized to each group. Compared to control, MT produced significant improvements in VASPI (Odds Ratio 5.12, \( P = 0.035 \)) and VASMOOD (Odds Ratio 11.6, \( P = 0.005 \)) with marginally significant improvements in VASPR (Odds Ratio 4.65, \( P = 0.056 \)). ML produced significant improvements in VASMOOD compared to control (Odds Ratio 5.76, \( P = 0.04 \)). There were no significant differences between ML and Control (on VASPI, \( P = 0.096 \), or VASPR, \( P = 0.439 \)) or ML and MT on all treatment outcomes. Qualitative data analysis from 17 interviews identified two prominent themes directly related to music: 1) ML and MT sessions offered many positive and few negative effects and 2) music therapists provide comfort beyond the music alone.

Conclusions: A brief individualized exposure to music, especially in the context of a MT encounter, diminishes pain in patients with SCD who are being treated for acute pain. MT may offer significant augmentation to current pain management strategies for adults with SCD. Research is ongoing into the long-term benefits of MT on patients’ daily pain and quality of life.

JSCDH-D-17-00048: Geographic Disparities among Hydroxyurea Medicaid Claims in Missouri

Authors: Anne Trolard, MPH Ben Cooper, MPH Allison King, MD, MPH, PhD

Affiliation: Washington University in St. Louis St. Louis, MO UNITED STATES

Abstract

Background: As part of the Heartland Sickle Cell Disease Treatment Demonstration Program Regional Collaborative, we sought to better understand the use of hydroxyurea (HU) in the state of Missouri. We hypothesized lower Medicaid claim rates for HU in rural vs. urban residents, and propose novel methods for visualizing claims data, both geographically and interactively, to better inform future educational efforts.

Methods: We requested a de-identified dataset of Medicaid patients with a sickle cell disease (SCD) diagnosis. We received three years of claim-level data including claim type; diagnosis, procedure, and drug codes; provider information; and patient demographics including zip code. We computed the number of HU prescriptions per patient per year. We used geographic information system (GIS) and data visualization software to display patient location with HU claims over time.

Results: A total of 900,450 claims were made on behalf of 1304 patients from 2013-2015. Patient ages ranged from <1 to 86 years old, with 53% female. Forty-six percent of claims were SCD-related. HU was prescribed at least once during the study period for 378 (29%) patients. There were no significant differences in HU use by sex. Zip code-level maps reveal higher densities of patients in urban vs. rural areas, along with disparities in HU prescription rates. Using the GIS tool global Moran’s I that measures spatial correlation, we found the distribution of HU rates was not random, controlling for the number of patients per zip code. The St. Louis area contained the highest patient counts, with HU prescription rates ranging widely from 0-100%, mean = 24.7%. While HU claims increased overall during the three-year period, a total of 90 patients with 2+ scripts in a previous year dropped off the following year.

Conclusions: While limitations exist in large administrative claims data, these Medicaid claims data were useful in studying the sickle cell patient population, particularly when geographic variables are present. GIS analysis revealed HU prescriptions varied geographically. As expected, rural zip codes with higher patient counts had lower HU prescriptions. However, even urban zip codes with similar patient counts had drastically different HU prescription rates. These results inform our efforts for future targeted education in dissemination and implementation efforts.
JSCDH-D-17-00051: Reduction of Pain Episodes Does Correlate with Geographic Origin in an International Cohort of Patients with Sickle Cell Anemia Treated with Hydroxyurea

Authors: Crawford Strunk, MD, Biree Andemariam, MD, Baba Inusa, MD, Fredericka Sey, MB ChB, Ivy Ekem, MD, Eugenia Vicky Asare, MD, Fatimah Farooq, BS, Rebekah Urbonya, BS, Duna Buttner, BS, Austin Novarra, BS, Lewis Graham, Gifty Dankwah Boatemaa, Charles Antwi-Boasiako, Ph.D, Daniel Ansong Antwi, PhD, Edeghonghon Olayemi, MD, Adetola A. Kassim, MD, Onika Rodrigues, MD, William Zempsky, MD, Connie M. Piccone, MD, Angela Rivers, MD, PhD, Deepa Manwani, MD, Imma Tartaglione, MD, Silverio Perrotta, MD, Laura Sainati, MD, Raffaella Colombatti, MD, PhD and Andrew D. Campbell, MD

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Background: Sickle cell anemia affects millions of people worldwide (WHO 2011), and is the most common single gene defect in the United States (Hassel Am J Prev Med 2010). It has been noted that different geographical areas of the world have a different sickle cell phenotype, each with their own characteristic laboratory values (Kleber Exp Rev Hematol 2010). Since 1984, hydroxyurea, a small molecule chemotherapeutic agent, has been used to treat patients with sickle cell disease (Brawley Ann Int Med 2008). This goal of this study was to evaluate whether improvement of pain episodes in patients on hydroxyurea is based on the patient’s geographic region and degree of Fetal hemoglobin elevation.

Methods The CASIRE group is an international collaborative group evaluating the clinical severity of patients with sickle cell anemia through a validated questionnaire, chart review and laboratory studies. Patients were enrolled on the CASIRE study after informed consent was obtained from either the parent or patient. The study
was approved at each participating institution’s IRB. A questionnaire was answered by the parents and/or patients, and baseline and current laboratory studies were collected. Patients were stratified by genotype (SS and Sβ0Thal), geographical region and hydroxyurea use. Two tailed paired t-test was used to compare significance of pain episode reduction. Analysis of variables (ANOVA) was performed for all groups and variables.

Results There were 263 patients in this study, (115 on hydroxyurea). Geographic region, fetal hemoglobin and last Hgb F are reported (table 1). Table two shows the number of pain episodes prior to hydroxyurea and in the last year. Groups are broken down into geographic region. Fetal hemoglobin levels are characterized by high, moderate or low. There were no statistical differences of any variable for any group. There was a reduction of pain episodes for most groups in the last year on hydroxyurea compared to prior to hydroxyurea. The reduction of pain episodes was not correlated consistently to geographic region or level of fetal hemoglobin induction.

Conclusions: Our data are consistent with our previous results that showed that reduction in pain episodes is not correlated with fetal hemoglobin induction in a general sickle cell population (ASH poster #2185; 2015). However, our current research shows that reduction of pain episodes does not correlate with geographic region and hence variability of fetal hemoglobin induction. This has several practical implications for clinical practice. First, induction of fetal hemoglobin should no longer be considered a marker of disease improvement; disease benefit should be monitored by clinical results. Second, patient education and medication reconciliation to monitor compliance should occur at every visit. Third, hydroxyurea therapy should be offered to every patient with sickle cell anemia. One of the limitations of our study is that not all data was collected for all patients, nor are all geographic regions represented. Obtaining more complete data from each geographic region may prove beneficial.
Table 1. Number of patients on HU with baseline and treated fetal Hemoglobin

<table>
<thead>
<tr>
<th>Region</th>
<th>No. (on HU)</th>
<th>Baseline Hgb F</th>
<th>Treated Hgb F</th>
</tr>
</thead>
<tbody>
<tr>
<td>East Africa</td>
<td>3 (1)</td>
<td>16.8</td>
<td></td>
</tr>
<tr>
<td>Central Africa</td>
<td>5 (2)</td>
<td>4.8</td>
<td>10.8</td>
</tr>
<tr>
<td>West Africa (excluding Benin Gulf)</td>
<td>8 (2)</td>
<td>14.5</td>
<td>25.8</td>
</tr>
<tr>
<td>West Africa (including Benin Gulf)</td>
<td>51 (16)</td>
<td>10.9</td>
<td>16</td>
</tr>
<tr>
<td>Sub-Saharan Africa</td>
<td>63 (19)</td>
<td>11.5</td>
<td>16</td>
</tr>
<tr>
<td>Middle East</td>
<td>5 (5)</td>
<td>21</td>
<td>24.5</td>
</tr>
<tr>
<td>Europe</td>
<td>19 (3)</td>
<td>13.2</td>
<td>22.9</td>
</tr>
<tr>
<td>America</td>
<td>88 (53)</td>
<td>9.9</td>
<td>13.6</td>
</tr>
<tr>
<td>Caribbean</td>
<td>21 (14)</td>
<td>11</td>
<td>15.5</td>
</tr>
</tbody>
</table>
Table 2. Number of pain episodes in patients on HU by region.

<table>
<thead>
<tr>
<th>Region</th>
<th>Prior to HU</th>
<th>In last year on HU</th>
<th>Level of Hgb F on hydroxyurea</th>
<th>2 tailed paired t test</th>
</tr>
</thead>
<tbody>
<tr>
<td>America (N = 81pts)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>12</td>
<td>5.5</td>
<td>Moderate (10-20)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>4.13</td>
<td>1.68</td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td># Requiring admission/year</td>
<td>6.05</td>
<td>2</td>
<td></td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Europe (N = 11)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>7.33</td>
<td>2.55</td>
<td>Moderate (10-20)</td>
<td>0.667</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>2</td>
<td>0.43</td>
<td></td>
<td>n/a**</td>
</tr>
<tr>
<td># Requiring admission/year</td>
<td>1.33</td>
<td>1.91</td>
<td></td>
<td>0.212</td>
</tr>
<tr>
<td>West Africa (N = 16)</td>
<td></td>
<td></td>
<td>High (&gt;20)</td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>9</td>
<td>4</td>
<td></td>
<td>0.019*</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>0.88</td>
<td>0.44</td>
<td></td>
<td>0.230</td>
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<tr>
<td># Requiring admission/year</td>
<td>1</td>
<td>1</td>
<td></td>
<td>0.298</td>
</tr>
<tr>
<td>Sub-Saharan Africa (N = 19)</td>
<td></td>
<td></td>
<td>Moderate (10-20)</td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>12</td>
<td>4</td>
<td></td>
<td>0.004*</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>1.1</td>
<td>0.37</td>
<td></td>
<td>0.268</td>
</tr>
<tr>
<td># Requiring admission/year</td>
<td>1.67</td>
<td>1.67</td>
<td></td>
<td>0.298</td>
</tr>
<tr>
<td>Middle East (N = 5)</td>
<td></td>
<td></td>
<td>High (&gt;20)</td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>68</td>
<td>13.75</td>
<td></td>
<td>n/a**</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>3</td>
<td>1.6</td>
<td></td>
<td>0.297</td>
</tr>
<tr>
<td># Requiring admission/year</td>
<td>3.2</td>
<td>1.4</td>
<td></td>
<td>0.137</td>
</tr>
<tr>
<td>Caribbean (N = 14)</td>
<td></td>
<td></td>
<td>Moderate (10-20)</td>
<td></td>
</tr>
<tr>
<td># Pain episodes/year</td>
<td>17.5</td>
<td>20</td>
<td></td>
<td>0.840</td>
</tr>
<tr>
<td># Requiring ED/year</td>
<td>4.5</td>
<td>1.5</td>
<td></td>
<td>0.934</td>
</tr>
<tr>
<td># Requiring admission/year</td>
<td>3</td>
<td>2</td>
<td></td>
<td>0.397</td>
</tr>
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</table>

**n/a= too few cases for significance calculation**
JSCDH-D-17-00038: *The Relationship between Self-Efficacy, Self-Management and Quality of Life in Adolescents and Young Adults with Sickle Cell Disease*

**Authors:** Lori E. Crosby PsyD Cara Nwankwo, BA James Peugh, PhD Lisa M. Shook, MA Naomi E. Joffe, PhD Emily McTate, PhD Maria T. Britto, MD, MPH

**Affiliation:** Cincinnati Children's Hospital Medical Center Cincinnati, OH UNITED STATES

**Abstract**

**Background:** Adolescents and young adults (AYA) with chronic diseases, such as sickle cell disease, (SCD) who have high levels of self-efficacy are more likely to engage in self-management behaviors and as a result, have better health outcomes including quality of life. While there is research in other chronic diseases, there is limited research exploring the relationship between these factors in AYA with SCD. This study examines these relationships in a sample of AYA with SCD. We hypothesized that AYA with SCD with high disease self-efficacy would report high levels of self-management and good quality of life.

**Methods:** AYA with SCD ages 13 - 21 completed measures of self-efficacy (Sickle Cell Self-Efficacy Scale), self-management behaviors (Transition Readiness Assessment Questionnaire – TRAQ5 and Allocation of Treatment Responsibility – ATR-Oral Medications Subscale), and sickle cell-related quality of life (Peds QL SCD Module) as part of a larger self-management intervention study at a pediatric hospital. Participants or their parents (participants <18 years) also completed a demographics form. Descriptive statistics summarized sample characteristics and Pearson correlations were used to examine relationships among self-efficacy, self-management and quality of life.

**Results:** Data from 30 participants was analyzed (M age = 16.4 ± 2.4; 53.3% male; 70% HbSS; 20% HbSC; 3.3% SβThal; 6.7% SD). There was a significant positive correlation between self-efficacy and the SCD Peds QL total score (r = 0.45, p = .02), Worrying II (r = 0.47, p = .01) and Communication I (r = .38, p = .04) and Communication II (r = .42, p = .02) subscales. There was also a positive significant correlation between self-efficacy and the TRAQ overall score (r = 0.45, p = .01), Appointment Keeping (r = 0.36, p = .05), Tracking Health Issues (r = 0.40, p = .03), and Managing Daily Activities (r = 0.43, p = .02) subscales.

**Conclusions:** Study results revealed that AYA with high self-efficacy reported high levels of self-management and good quality of life; as well as fewer worries about SCD pain and management, and less difficulties communicating about SCD symptoms, managing appointments and insurance, tracking symptoms, and managing daily activities. Although future studies are needed to confirm study findings,
results provide some direction for intervention. For instance, self-management interventions that include teaching AYA to manage health appointments and daily activities, track symptoms, and talk with others about symptoms may improve self-efficacy and health outcomes and quality of life in AYA with SCD.

References


Discovering Normal: Life after Hematopoietic Stem Cell Transplant for patients with Sickle Cell Disease

Authors: Kirshma Khemani, M.D. Kasey Bates, CCRP Diana Ross, MSN, RN Ann Haight, M.D. Cynthia Sinha, PhD Nitya Bakshi, MBBS, MS Lakshmanan Krishnamurti

Affiliation: Emory University Atlanta, Georgia UNITED STATES

Background: Sickle Cell disease (SCD) is associated with severe complications, impaired quality of life and the risk of premature mortality. Hematopoietic stem cell transplant (HSCT) is the only therapeutic option with a curative intent for patients with SCD. Excellent overall survival and disease-free survival has been reported after HSCT in matched-sibling donors. There is, however, a paucity of data on patient and caregivers' perspective on the impact of a successful HSCT for SCD. Our objective was to determine how HSCT impacted the lives of patients and caregivers from their perspective.

Methods: We completed a qualitative study using semi-structured interview guide of patient-caregiver dyads as well as two focus group sessions of adult long-term survivors of HSCT to elicit their perspective on life events after HSCT. They were recorded and transcribed verbatim. Transcripts were coded and analyzed for emerging themes using NVivo 10.0. We have previously reported our findings on the decision-making process and experiences with HSCT from the patient and caregiver perspective. (ASH Abstract #2393).

Results: We enrolled eleven patients-caregiver dyads (n=6, female patients, n=10, mothers) in the qualitative interviews. We conducted two focus groups with five (n=2, females) and seven (n=3, females) participants in each group, respectively. The major emerging theme reflected the dramatic impact HSCT had on many aspects of life. Patients reported that the most remarkable change was the decrease in acute pain crisis, and the ability to participate in normal life without the limitations imposed by SCD related treatments, complications, and restrictions. School-aged patients voiced excitement to finally be able to participate in normal school, sports, and social activities. Some young adults attempted to compensate for lost time by undertaking academic challenges or even indulge in competitive extreme sports. Both patients and caregivers noted that being cured of SCD resulted in a desire to discover a normal life, provided hope, and an opportunity to plan for the future.

Conclusion: Following cure of SCD by HSCT, patients and their families finally felt liberated from the burden of disease. They perceived it as a new beginning, a “re-birth” of a life without suffering, with hope, and expectations for the future.
JSCDH-D-17-00006: A Phase 2 Safety Study of SANGUINATE in Patients with Leg Ulcers

Authors: *Peter Buontempo, Lineth Lopez MD, Gladys Maria Paulino MD, and Hemant Misra PhD.

Affiliation: *Prolong Pharmaceuticals South Plainfield, New Jersey UNITED STATES

Abstract

Introduction Leg ulcers are a serious and debilitating complication of sickle cell disease (SCD). It is estimated that leg ulcers develop in 10% or more of people with sickle cell disease during their lifetime. Chronic tissue hypoxia, hemolysis and inflammation result in a cascade of events leading to progressive de-vascularization and tissue necrosis resulting in chronic wounds that show no tendency to heal after months of appropriate treatment.

SANGUINATE is an oxygen carrying agent with anti-inflammatory activity. A safety study was undertaken in SCD patients with chronic leg ulcers to determine the safety of this investigational drug administered in as a once weekly infusion.

Methods: The study was conducted in Panama and the Dominican Republic. This was an escalating, repeated-dose, open-label, Phase 2 study to test SANGUINATE at 320 mg/kg (8 mL) in subjects suffering from leg ulceration associated with SCD. All enrolled subjects underwent a 3-week Run-In Period, during which they received standard of care treatment for the wound management.

During the Treatment Phase subjects were assigned sequentially to Cohort 1 or Cohort 2. Cohort 1 received 4 doses, once-weekly, 2-hour intravenous (IV) infusions of SANGUINATE 320 mg/kg. Following the completion of Cohort 1, the safety findings were reviewed prior to initiating Cohort 2. Cohort 2 received once-weekly infusions for 6 weeks. In addition to the study drug, subjects continued to receive standard of care during the Treatment Period. One week after the end of the Treatment Phase, subjects returned to the study center for a Final Visit.

The following assessments were done:

- Safety: Safety was assessed by recorded adverse events (AEs), laboratory assessments (hematology, chemistry, and urinalysis), vital signs, concomitant medications, and 12-lead electrocardiograms (ECGs).
- Efficacy: Wound pain, wound appearance and condition, wound size, wound vascular status (Venous Clinical Severity Score; VSCC)
- Quality of Life: Quality of life was assessed using the Short Form-12 v2 Health Survey (SF-12).

Results: The administration of once-weekly infusions of SANGUINATE was well tolerated. 2/10 patients report treatment emergent adverse events considered related to study drug. Mean changes for blood pressure did show some increases due to oncotic and colloidal nature of drug, but there was not a consistent
pattern to those changes. Changes in ECG intervals were seen in a few subjects, but those changes were not considered clinically meaningful. There were no clinically meaningful changes in laboratory values, physical examinations, or concomitant medications.

There were no statistically significant changes from Baseline in leg ulcer pain and wound surface area for either Cohort. All of the wound assessments remained relatively consistent throughout the study. There were slight decreases in total VCSS at most time points, indicating slight improvement in vascular status. Results were similar for the individual scores.

**Conclusion:** The administration of 4 or 6 once-weekly infusions of SANGUINATE at a dose of 320 mg/kg was generally well tolerated. Slight improvements in total and individual VCSS are promising and may warrant further study.

**JSCDH-D-17-00039:** **Comparison of Two Methods of Transfusion for Stroke Prevention in Sickle Cell**

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**Abstract**

**Background:** Chronic blood transfusions are essential supportive care for sickle cell patients at high risk for morbidity and mortality due to stroke. In our pediatric comprehensive sickle cell center we support chronic transfusion therapy with rapid manual partial exchange transfusion (RMPET) using a single access central line port. We lack an adult program, and upon transition these patients would be provided simple transfusion (ST) in an adult ambulatory setting. We sought to compare differences in RMPET versus ST, specifically comparing hematologic factors between the two methods of transfusion. We also determined nursing time and patient satisfaction for both procedures.

**Methods:** We included nine (5 male, 4 female) chronic transfusion patients at the Children’s at Erlanger Infusion Clinic. All patients were consented to a prospective observational cohort study. Each patient was randomly assigned with a blinded envelope to either of the two methods. Group 1 received RMPET for a total of six months with a crossover to simple transfusion for six months; Group 2, six months of simple transfusion with a crossover to RMPET for the next six months. There was a three-month wash out period to stabilize the blood volume of transfusion to each patient. All patients were between 3 and 25 years of age, diagnosed with hemoglobin SS or Sbeta0-thalassemia and were receiving chronic exchange for stroke prevention. Exclusion criteria were a diagnosis of SC disease or transfusion for priapism. We optimized therapy to achieve a post transfusion goal of Hemoglobin S<30% and hemoglobin <12. We hypothesized there would be no statistically significant difference between the two methods of transfusion.
Results: After the wash out period, blood volume amounts were equivalent in the two groups. The straight method group had higher levels of hemoglobin and hematocrit (p=0.043). With oral iron chelation, there was no significant difference in ferritin burden between groups. No significant difference was noted in the post transfusion hemoglobin S percentage. Interestingly, although the average time for RMPET was 179 minutes versus 94 minutes for ST, neither nurse nor patient satisfaction was significantly different between the two methods.

Conclusions: In our comprehensive sickle cell clinic setting, we have switched to utilizing straight transfusion for our patients rather than the nurse-intensive method of RMPET to prevent stroke in our population of children. We now have a method to recommend to the adult ambulatory center accepting our transitioning patients for lifelong transfusion to prevent stroke.

JSCDH-D-17-00049: Successful Implementation of Hydroxyurea in a Single Pediatric Sickle Cell Center

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Background: The benefits of Hydroxyurea (HU) in sickle cell disease (SCD) have been well documented. Compelling results from adult longterm followup studies and the BABY HUG trial expanded the use of HU for all patients with severe forms of SCD, including very young children. However, barriers to HU usage remain and HU continues to be underutilized in the community.

Objective: Determine the feasibility and effectiveness of universal hydroxyurea implementation in a pediatric sickle cell population.

Design/Method: In October 2011, the Center for Cancer and Blood Disorders of Northern Virginia initiated a program to place all patients with severe SCD on HU starting at 9-12 months of age. An IRB-approved longitudinal database was launched in 2011 to track clinical status and outcomes. Data were analyzed for the effectiveness of HU implementation from 2011-2015. Patient outcomes included total Hgb, HgbF, hospitalizations, ED visits, and transfusions, which were assessed for patients with severe SCD in years 2011, 2013, and 2015.

Results: Approximately 250 patients up to age 25 were followed. Over 60% of the cohort had Hgb SS,
HgbSbeta0thalassemia, HgbSO\textsuperscript{Arab}, Hgb SC\textsuperscript{Harlem}, and were evaluated.

HU prescription rate increased from 29%, to 84%, then to 91% for 2011, 2013, and 2015. Average Hgb increased from 8.4g/dL to 9.4g/dL (p<0.01), to 9.5g/dL. The percentage of patients with Hgb>9g/dL rose from 25% to 57% (p<0.01), to 67%, and 33% of patients had Hgb>10g/dL in 2015. Over 90% of patients on HU showed longitudinal improvement in Hgb from 2011 to 2015. Average HgbF were 14%, 24% (p<0.01), and 23% in 2011, 2013, and 2015. The percentage of patients with HgbF>20% were 24%, 63% (p<0.01), and 60%, while 27% had HgbF>30% in 2015. Hospitalizations decreased more than 3-fold from 0.85 to 0.36, then to 0.24 admissions/person-year (p<0.01), and the percentage of patients hospitalized decreased from 57.9% to 40.3% (p=0.0024), then to 31.5%. Pain remained the most common cause of hospitalizations. Chronic transfusion rate decreased from 11% to 7% to 2% (p=0.0003), and patients receiving sporadic transfusions decreased from 27% to 18% to 8% (p<0.01). There was no significant change in the rate of uncomplicated ED visits that did not result in hospitalization.

**Conclusion:** Rigorous HU prescription and enforcement resulted in significant improvements in Hgb, HgbF, hospitalizations, and transfusion rates within 2 years that were sustained for the subsequent 2 years, demonstrating feasibility and effectiveness of widespread HU implementation in the pediatric sickle cell community.

**JSCDH-D-17-00025:** *Older Adults with Sickle Cell Disease are Skeptical About Hydroxyurea: Results of a Qualitative Study*

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**Background:** Despite decrease in morbidity and mortality with Hydroxyurea (HU), the uptake of HU in adults with SCD is poor. Poor uptake of HU the result of a combination of both physician and patient related factors. In this study, we investigated attitudes of adult patients towards the purpose, side effects, and risks and benefits of taking HU.

**Methods:** We analyzed qualitative interviews of adult SCD patients from a geographically diverse population recruited from national conferences and local clinics. A semi-structured open-ended interview guide was used to collect data. Audio recordings were transcribed verbatim. Transcripts were coded using qualitative content analysis with NVivo 10.

**Results:** Age of the 95 participants ranged from 18 years to 67 years old. Female = 71. All participants identified as African American except one who identified as “other” and one who
identified as “multiracial.” Approximately 50% of the patients reported that they were currently on HU. The younger participants, 18 to 31 years, were likely to have started HU when they were minors. They reported that the decision to accept a physician recommendation to start HU was made by their parent. Younger participants generally described the purpose of HU as intended to improve “blood counts” thereby decreasing crises and hospital stays. They articulate their decision to use HU in terms of “promise” of less pain and more energy. They are hopeful that HU is “supposed to help” and thus are focused on the potential for successfully managing SCD complications rather than focused on the side effects from HU. The older participants, 31 to 67 years old, while aware that HU would potentially decrease crises, saw it as but one of a few unsatisfactory options. They expressed much more ambivalence about HU and were seeking new treatments, for SCD. The older participants who were not taking HU, expressed the most anxiety concerning long-term side effects. They were concerned that while their disease status, bad as it may be, was the “known” the long-term effects of taking HU was the “unknown.” Participants were skeptical that research has identified all side effects from long-term use of HU.

Conclusion: These data suggest that there are significant differences by age in adult SCD patients' understanding of the purpose and risks and benefits of HU. Decision aid tools should incorporate this awareness of age differences so that older patients are well-informed on the full range of available treatment options.

JSCDH-D-17-00017: Barriers to Care and Hydroxyurea Adherence in Children with Sickle Cell Disease

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Background: Children with sickle cell disease (SCD) and their families report a number of barriers to taking hydroxyurea as prescribed (adherence). These include logistics (e.g. coming to clinic, liquid only available at specific pharmacies), forgetting, competing responsibilities, and perceptions about hydroxyurea and sickle cell disease (e.g. may take 3-6 months to experience benefits). An improved understanding of how these barriers impact hydroxyurea adherence is essential to developing effective adherence-related interventions for this population. The goal of the current study was to assess the relationship between barriers to care, illness perceptions and hydroxyurea adherence in children with SCD taking hydroxyurea. We hypothesized that participants experiencing more barriers to care would
report negative perceptions of SCD and lower adherence to hydroxyurea.

**Methods:** Patients/families completed measures as part of a larger hydroxyurea adherence study. Measures included a demographics survey (age, gender, hemoglobin type), the Brief Illness Perception Questionnaire\(^3\) (IPQ), two items of self-reported adherence from the Medical Adherence Measure\(^4\), and the Barriers to Care Questionnaire\(^5\) which assesses barriers to treatment including cost/logistics, health navigation skills, negative healthcare experiences, and health care knowledge. We used descriptive statistics to summarize sample characteristics and self-reported adherence and Spearman correlations to examine relationships between barriers to care, illness perceptions, self-reported adherence, and demographics.

**Results:** Analyses of data from 21 participants (Mean age = 12.9 ± 5.8; 52.4% Female; 100% African-American; 100% HbSS) revealed no relationship between age, gender or hemoglobin type and barriers to care (BCQ total score). In addition, experiencing treatment barriers was not related to self-reported adherence (89%). There was a significant inverse relationship between barriers to care and overall illness perceptions (IPQ total score) such that higher barriers were associated with more negative illness perceptions. With respect to subscales, significant Inverse relationships were found between barriers to care total scale and IPQ consequences (illness has consequences on life), identity (illness/symptoms experienced), and emotional representation (how much control over illness) subscales.

**Conclusions:** As predicted, in our sample of children with SCD, participants reporting more barriers to care had more negative perceptions of SCD. However, those reporting more barriers to care did not report lower adherence to hydroxyurea. Additional studies to improve our understanding of how barriers to care impact participant/family treatment decisions are needed. Next steps are to continue data collection including information on specific barriers to hydroxyurea adherence and electronically monitored adherence rates.

**References**
**JSCDH-D-17-00041: Creation and Maintenance of a Hematology Support Group for Adolescents and their Parents: Successes, Challenges, and Lessons Learned**

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**Abstract**

**Background:** Support groups can be invaluable to adolescents with chronic illnesses such as sickle cell disease (SCD) and other hematological disorders. They can provide social, emotional, and disease-related benefits. The idea of the Hematology Teen/Parent Support Group originated from a series of focus groups with adolescents with SCD and their parents with the purpose of gathering preliminary data to evaluate our transition to adult care program. During these focus groups, parents expressed interest in having a space where (a) they could meet regularly with other parents of adolescents with a hematological disorder and (b) their adolescents could meet and obtain support from peers. The objective of this abstract is to describe the process of creating and maintaining the group, including successes, challenges, and lessons learned.

**Methods:** A Hematology social worker surveyed Hematology patients and their families regarding their interest in a support group. The Hematology licensed teacher presented the survey findings to the Hematology department to demonstrate the need for and patient/family commitment to participating in a support group for adolescents with hematological disorders. Using the survey results, we created a support group for adolescent Hematology patients (SCD and hemophilia) and their parents within our large pediatric research hospital. Recruitment strategies consist of approaching adolescents and their families during medical follow-up visits, mailings, and phone calls to families who have either attended or expressed interest in attending future groups.

**Results:** Approximately 8-9 adolescents aged 13-18 years (with an even distribution of males and females) and their parents have attended per month, which has been meeting since March 2015. The facilitators include a social worker, licensed teachers, a psychologist, and a psychology postdoctoral fellow. The group’s needs and goals are periodically assessed to ensure continued effectiveness. Some challenges have been recruitment and group maintenance. However, there have been many successes including the bonds that have formed between group members and a consistent number of participants. Lastly, facilitators have learned how critically important multidisciplinary involvement and institutional funding and support is to the group’s growth.

**Conclusions:** A monthly support group for adolescents with SCD and their
parents is feasible and sustainable. It can be a beneficial resource for families with a child with a hematological disorder, but formal measurement of its benefit has not yet been conducted. Future directions include formally evaluating the group’s effectiveness on psychosocial and disease-related outcomes and starting targeted support groups for younger patients and their parents.

HEALTH SERVICES RESEARCH

JSCDH-D-17-00002: A Pilot Study of Sickle Cell Anemia in the Belizean Population

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Abstract

Background: Sickle Cell Anemia (Sickle Cell Disease) is an inherited disease resulting from a genetic mutation in the hemoglobin protein found in red blood cells. Screening is a requirement in the United States and in U.S. territories, and is considered a component of routine prenatal care. In resource-limited countries such as Belize, there are no screening programs in place for testing newborns for Sickle Cell Anemia, and the disease is largely undefined. Children often go undiagnosed until they exhibit clinical symptoms. Untreated Sickle Cell Anemia in children under the age of 5 can lead to poor clinical outcomes. Oftentimes, those suspected of having the disease obtain diagnostic testing from a foreign country, and the test frequently used is the Sickle Prep Test. While the Sickle Prep Test is able to identify the presence of hemoglobin mutations, it cannot differentiate between sickle cell disease and sickle cell trait, a distinction which has profound clinical implications. A new technology, the Sickle SCAN test, utilizes a chromatographic, immunologic approach to qualitatively identify the presence of select variants of the hemoglobin protein (HbS, HbA, HbC), thereby allowing clinicians to differentiate between sickle cell disease and sickle cell trait. This test is a powerful tool that it is cost effective and timely; it does not require complicated testing equipment, and can disclose one's hemoglobin genetic profile in under 6 minutes.

Methods: 87 patients were enrolled and tested for sickle cell disease and sickle cell trait in the towns of Dangriga and Hopkins, Belize. Testing took place over the course of 4 days. A survey was administered to collect key demographic information regarding participant’s knowledge about Sickle Cell Anemia, past diagnosis, and family history of disease.
Results: 13% were found to have sickle cell disease (n=12), and 25% were found to have the trait (n=22). For those with the disease or trait, the majority were found to belong to the Garifuna ethnic group. 26% of the participants had no knowledge of Sickle Cell Anemia. It was also reported that 51% had a family member with the disease, and 23% were unsure whether a family member had the disease.

Conclusions: This pilot study demonstrates the feasibility of using the Sickle SCAN test to gather knowledge about the prevalence of Sickle Cell Anemia in a population where the disease remains largely undocumented.

JSCDH-D-17-00024: Applying Sickle Cell Disease Quality Metrics to an Integrated Care System

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Abstract

Background: To date, there are no standardized, well-accepted, quality metrics that guide care for adults with sickle cell disease (SCD). The primary objective of this study was to evaluate metrics that are in use at the Adult Sickle Cell Disease Program at Johns Hopkins Hospital (JHH) and to determine if these metrics can be applied at Kaiser Permanente Mid-Atlantic States (KPMAS), a developing adult sickle cell disease program within an integrated healthcare system.

Methods: We performed a retrospective cohort study of 148 KPMAS and 324 JHH patients from January 1, 2014 – December 31, 2015. Demographics, genotype and data on 3 quality metrics (yearly screening labs, vaccinations and hydroxyurea prescriptions written) were collected from electronic health records (EHR).

Results: Patients at JHH were younger than those as KPMAS (median age 34 and 44 respectively) and more likely to have hemoglobin SS disease (65% and 28% respectively). Yearly lab performance is shown in the figure. Given that only vaccinations administered within our institutions are included, 80% of KPMAS patients received pneumococcal and 75% received flu vaccinations compared to 80% and 48% at JHH. 26 of 62 (42%) of patients at KPMAS and 115 of 261 (44%) at JHH with hemoglobin SS or S-thal were written a hydroxyurea prescription over the study period. This data includes all patients with those genotypes and not necessarily those who meet the eligibility criteria in the NHLBI guidelines. Only 65% of KPMAS and 53% of JHH patients written a prescription for hydroxyurea were provided scripts to cover at least 6 months over the two-year study period.
Conclusions: Using the number of prescriptions written for hydroxyurea (and not more stringent hydroxyurea refill data), it is clear that interventions to improve adherence to hydroxyurea should be a focus. Developing dashboards to monitor adherence to guideline based care for those with SCD has limitations but there is an opportunity to use the EHR to refine and implement this to improve access to high quality care for those with SCD. One limitation that will have to be addressed is data recording, including vaccinations that happen outside our institutions.

JSCDH-D-17-00034: Case study of impact of sickle cell day unit on adult patient outcomes post pediatric transition

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Abstract

Background: The goal of this study is to evaluate the impact of the implementation of a sickle cell day unit (SCDU) on health care utilization (HCU) patterns and health outcomes of patients transitioning from pediatric to adult care pre- and post-implementation of a SCDU. Specifically, we will examine any changes that may have occurred in the use of acute care services since the implementation of a SCDU with a specific focus on the number and length of emergency department (ED) visits, hospital admissions, and re-hospitalizations. This study will also explore associations with other important health outcomes (e.g., reticulocyte counts, ferritin levels) for this population.
Methods: The sample consists of 35 patients, ages 19 to 25 years (M = 22.48, 54% female), diagnosed with sickle cell anemia HbSS. De-identified data were extracted from electronic health records. For each hospital visit, laboratory results were analyzed. The requisite medical chart review for this analysis is in progress; findings from the complete analysis of this data will be presented. Data analyses will be conducted with the use of descriptive statistics to describe HCU and other health outcomes (e.g., ED visits, SCDU visits, hospital admissions, length of stay, etc.). All analyses will be conducted using Chi-square and t-test analyses to compare HCU and health outcomes for patients pre and post-implementation of the SCDU.

Hypotheses: The patients who transitioned from pediatric to adult care prior to the implementation of the SCDU will have an overall higher rate of HCU as compared to those patients who transitioned after the day unit was established.

Conclusion: To our knowledge, this is the first study to analyze the impact of the implementation of a SCDU on HCU in patients transitioning form pediatric to adult care. This research is warranted given previous findings that indicate high mortality risks in the young adult SCD population, particularly shortly after transition (Quinn et al., 2010). Young adults (18-30 years old) are also among the highest users of health care services. Armed with the knowledge of the impact of SCDU on HCU for newly transitioning patients, wider implementation of SCDUs in hospitals may be instrumental in ameliorating negative health outcomes for young adults with SCD.

JSCDH-D-17-00013: Patient and caregiver understanding of shared decision making for sickle cell disease: A qualitative study

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Abstract

Background: Shared decision-making (SDM) is a collaborative approach between patients and healthcare providers (HCPS) to determine patient treatment. There are three basic elements of communication for SDM: 1) A decision is needed, 2) Risks, benefits, and efficacy are understood, 3) Provider recommendations as well as patient values and preferences are considered (Légaré & Witteman, 2013). The objective of this study was to understand patient interpretation of SDM.
Methods: We analyzed qualitative interviews of patients and caregivers from a geographically diverse population recruited from national conferences and local clinics. A semi-structured open-ended interview guide was used to collect data. Audio recordings were transcribed verbatim. Transcripts were coded using content analysis with NVivo 10.

Results: We enrolled 49 participants, 48 were African American, median age 37 (range 19 to 66), and 41 were female. Of the 43 that had at least some college, 10 held a bachelors, and 16 were post-graduates. Most participants never heard of the term SDM nor do they explicitly understand its meaning. For many who have heard of it, SDM represents shared responsibility between the patient/parent and the physician to make an informed decision about healthcare needs. All participants indicated a strong desire to be involved in SDM and many noted that patients have the final say. The role of physicians is to introduce treatments options or test procedures, including risks and benefits. The role of patients/parents is to discuss and understand these risks and benefits. Nurses are more involved with in-patient needs. Social workers should provide support and address barriers to care, such as cost and transportation. Most identified a need to do their own research, which included talking with other patients. Family members are not directly involved in SDM but should offer support and provide anecdotal medical history. Most participants learned to make medical decisions out of necessity as they became adults or had an infant with sickle cell disease (SCD). Most expressed themselves as being fairly confident they make good decisions stating validation through outcomes such as improved blood counts and no side effects. They also cited their health as a factor in confidence, stating this was of the utmost importance.

Conclusions: Patients with SCD and their parents in this study expressed a desire to be part of the SDM process. They believed that the physician’s role is to give information about treatment options and risks and benefits and it is for the patient to decide.

Objective: Emerging research indicates that medication errors are common in the outpatient and home settings. Our objective was to identify interventions to reduce errors in hydroxyurea (HU) use at home among children with sickle cell disease (SCD).

Methods: In collaboration with patients with SCD and their parents, we employed a failure modes and effects analysis, a systematic method used commonly by hospitals to identify how a process can fail, to prioritize failures and identify interventions. We focused on the use of HU after a change in the dose or a new prescription, because in our prior research this process exposed high rates of error. Six parents and one young adult developed a map of the current process for using HU at home and identified potential failure modes (what can go wrong) at each step in the process. To determine the relative impact of the failures, four different parents answered Likert scale questions about the likelihood of occurrence and ability to detect each of the failure modes. Two clinicians (LC, KW) assigned a Likert scale score for severity of injury that could occur. To identify the top-ranking failure modes, we multiplied the three Likert scale numbers (likelihood of occurrence, ability to detect failures and severity). A separate intervention development team, made up of 3 parents and one young adult, identified interventions to prevent each of the top-ranking failures.

Results. 11 parents and one young adult using HU at home participated in the study. Top ranking failure modes (in order) were: (1) forgetting when to give the medicine, (2) the patient/family not understanding physician instructions about the HU dose, (3) the doctor and others in the clinic telling the patients/family different doses of HU to give, (5) a change of pharmacy, and (6) measuring the wrong amount of medication to give. Families proposed several interventions, including reminders, text messaging to check doses given at home, changes to the medication education process in clinic, a tracker/calendar which clinicians give parents to use at home when giving medicines, and a questionnaire that patients/parents could complete prior to appointments to discuss failures in HU use.

Conclusions. Parents and patients identified several high priority failures that can lead to error in HU use. A failure modes and effects analyses effectively engaged parents in intervention development; we were able to combine online and in-person participation to reduce participant burden.
<table>
<thead>
<tr>
<th>Failure Mode</th>
<th>Likelihood of Occurrence</th>
<th>Detectability</th>
<th>Severity Rating</th>
<th>Product</th>
</tr>
</thead>
<tbody>
<tr>
<td>Notice it’s time to give medicine: Forget what time to give medication</td>
<td>4.5</td>
<td>5.3</td>
<td>3.5</td>
<td>82.6</td>
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<tr>
<td>Doctor changes dose/gives new prescription: Patient/family does not understand instructions</td>
<td>3.8</td>
<td>3</td>
<td>7</td>
<td>78.75</td>
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<tr>
<td>Doctor changes dose/gives new prescription: Miscommunication—Dr. and clinic team tell the family 2 different doses/prescriptions</td>
<td>4.8</td>
<td>2.5</td>
<td>6</td>
<td>71.3</td>
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<tr>
<td>Pick up medication at pharmacy: Changes pharmacies</td>
<td>3.5</td>
<td>6.5</td>
<td>3</td>
<td>68.3</td>
</tr>
<tr>
<td>Notice it’s time to give medicine: Caregiver/patient forgets and does not give medication</td>
<td>3.8</td>
<td>3</td>
<td>6</td>
<td>67.5</td>
</tr>
<tr>
<td>Draw up medicine with syringe/take out proper number of pills:</td>
<td>2.8</td>
<td>3.5</td>
<td>7</td>
<td>67.4</td>
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<td>Take out wrong amount of pills</td>
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JSCDH-D-17-00040: Type I Diabetes and Sickle Cell Disease a Case Series of Pediatric Patients at Rainbow Babies & Children’s Hospital

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Abstract

Background Type 1 Diabetes (DM1) is rarely described in conjunction with sickle cell disease (SCD). The few published case reports infrequently report testing for antibody-positive (Glutamic Acid Decarboxylase (GAD65), Insulinoma Antigen 2 (IA2)) disease. Furthermore, the presence of SCD affects HbA1c measurements and provides an additional challenge in DM1 management. Fructosamine, a validated surrogate marker of short-term blood glucose control, is used for monitoring purposes but is not ideal.

Objective: To identify pediatric patients with both DM1 and SCD cared for at UH Rainbow Babies & Children’s Hospital.

Design/Method: A retrospective chart review of pediatric patients with a diagnosis of SCD, any genotype, and DM1 was performed over a 3-year time period.

Results: From April 2013 to November 2016, approximately 1200 patients were followed for DM1 at our institution. During that same time, about 250 children were followed routinely for SCD. We identified three African American males with SCD and DM1, all of whom presented in diabetic ketoacidosis (DKA) at their initial DM1 diagnosis.

Patient 1: 9-year-old with HbSS disease complicated by dactylitis, vaso-occlusive crises (VOC), acute chest syndrome
(ACS), and splenic sequestration; diagnosed with DM1 at 4 years of age; GAD65 positive (IA2 not tested).

Patient 2: 9-year-old with HbSS disease complicated by pneumococcal sepsis, dactylitis, VOC, splenic sequestration, cholecystitis, and iron overload secondary to chronic transfusions for an abnormal transcranial doppler (TCD); diagnosed with DM1 at 9 years of age; GAD65 and IA2 positive. Of note, this patient has had previous HLA typing significant for DRB1*13:01 and DQB1*06:09, a combination that may be associated with DM1.

Patient 3: 5-year-old with HbSC disease without significant complications; diagnosed with DM1 at 4 years of age; GAD65 and IA2 negative.

All three patients have had persistently elevated fructosamine levels despite being on adequate doses of insulin.

**Conclusions:** SCD poses potential management difficulties in DM1 evaluation and treatment. Fructosamine levels in our patients remained elevated on insulin, either reflecting compliance issues or lack of an established reference range in the SCD population.

Moreover, the combination of SCD and DM1 is less common in our population than would be expected based on population data. It is possible that the inheritance of protective HLA haplotypes prevents SCD patients from developing DM1, which is tightly associated with certain class II HLA genes. It is also possible that protective structural alterations to the red blood cells might offer increased resistance to environmental exposures and decreased autoimmune dysregulation, both of which have been implicated in the pathogenesis of DM1.
**JSCDH-D-17-00005: Long-Term Dosing in Sickle Cell Disease Subjects with GBT440, A novel HbS polymerization inhibitor**

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**Affiliation:** Global Blood Therapeutics South San Francisco, CA UNITED STATES

**Abstract**

**Background:** Sickle cell disease (SCD) is caused by polymerization of Hemoglobin S (HbS), resulting in hemolysis and vaso-occlusion. No therapy achieving pancellular, direct inhibition of HbS polymerization is available. GBT440 is a novel small molecule which increases hemoglobin oxygen affinity and inhibits HbS polymerization and prevents sickling in vitro.

**Methods:** This randomized, placebo-controlled, double-blind, phase I/II study enrolled (healthy volunteers) HV and SCD patients (HbSS and HbSB°). The study was conducted in three parts: Part A, single ascending doses, Part B, multiple ascending doses for 28 days and Part C, 90-day dosing. Longer term dosing (up to 6 months) is being evaluated. The primary endpoint was safety. Secondary endpoints included PK, PD and hematological effects.

**Results:** As of 7Nov2016, 56 SCD patients had been enrolled: 38 completed Part B (10 at 500mg; 12 at 700mg; 6 at 1000mg; 10 received placebo [pbo]); and 16 have completed or are ongoing in Part C (6 at 700mg: 6 at 900mg; 4 on pbo. Data presented include efficacy for SCD patients who have received multiple doses of GBT440 for 3 to 6 months (Part C) and safety for all SCD patients who received multiple doses of GBT440 (Part B and C). Part C includes 65% male; 18% on hydroxyrea (HU); 35% had 1 or more painful crises requiring hospitalization in the prior year; median age was 36 years (range, 18 to 53). GBT440 was well tolerated for up to 6 months of dosing. There were no drug-related severe or serious adverse events; all treatment-related AEs were Grade 1 or 2. The most common treatment-related AEs were headache, and gastrointestinal disorders. No sickle cell crises events occurred while on study drug.
All SCD patients receiving GBT440 for up to 6 months have shown hematologic response. Significant portion (46%) of subjects demonstrated a clinically significant increase in Hb (>1g/dL) increase vs 0% of placebo patients (Figure 1), p=0.006.

**Conclusions:** Long-term dosing of GBT440 up to 6 months continues to show favorable safety profile. GBT440 resulted in marked and sustained reduction in clinical markers of hemolysis and an increase in hemoglobin. These results are consistent with inhibition of HbS polymerization leading to decreased RBC damage, improved RBC lifespan and tissue oxygen delivery, and support further investigation of GBT440 in the recently initiated Phase 3 HOPE Clinical Study.

**Figure 1:** Significant Proportion of Patients Achieve Large Hb Response (>1 g/dL)

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**JSCDH-D-17-0008:** *The 9-item Sickle Cell Disease Severity Measure (SCDSM): A novel measure of daily SCD symptom severity developed to assess benefit of GBT440, an experimental HbS polymerization inhibitor*

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**Abstract**
Background: GBT440 inhibits HbS polymerization and reduces hemolysis, and is a promising treatment for Sickle Cell Disease (SCD). The traditional clinical endpoint, vaso-occlusive crisis (VOC) requiring healthcare utilization, is not a sensitive measure of the daily burden of symptoms in patients (the “tip of the iceberg” of severe symptom exacerbations) and poses a barrier to development of new treatments for SCD.

The objective was to develop a sensitive measure to detect treatment-related improvements in daily symptoms and exacerbations that define the disease. Existing SCD measures focus on distal impact, not on the core signs and symptoms of disease.

Methods: The content of the new measure was derived from 1-on-1 open-ended concept elicitation interviews in 56 adults and 10 adolescents with SCD in the US and UK. Participants were aged 12-63 years, 64% female, 33% had 1-3 and 48% had 4 or more VOC in the previous year requiring urgent care.

Interview transcripts were coded to identify the most bothersome and frequently mentioned concepts related to both “good” and “bad” days. As hypothesized, patients reported having crisis days more frequently than those crises requiring healthcare utilization (traditional VOC endpoint).

Results: After eliciting an initial pool of items using open-ended interviews, the items were administered to a small cohort of SCD patients. Revisions were made after analyses and re-administered to 50 SCD patients. Qualitative and quantitative analyses provided evidence that a set of 9-items demonstrated content validity in adult and adolescent SCD patients to produce a score to measure the full range of sickle cell disease severity.

The final content includes items specific to pain, fatigue, concentration and breathlessness. Evidence supports the derived estimate as a reliable and valid measure of SCD symptom severity and providing the ability to differentiate baseline symptoms from severe symptoms.

Patient responses to the 9-SCDSM items are combined to generate a single daily estimate of SCD symptom severity.

Conclusions: SCD patients have a high burden of daily symptoms, with severe or “crisis” days occurring more frequently than traditionally defined VOC. The 9-item SCDSM is a promising new measure of daily SCD symptom severity developed to be fit for purpose to determine the treatment effect of new drugs on potential improvement in baseline symptoms and/or prevention of symptom exacerbations. SCDSM will be used to explore the clinical benefit of GBT440 in the Phase 3 HOPE Clinical Study.
**JSCDH-D-17-00016: Safety and Tolerability of PF-04447943 Across a Clinical Trial Program Including 267 Patients**

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**Abstract**

**Background:** Current treatment options (eg, hydroxyurea, chronic blood infusions, and bone marrow or stem cell transplantation) for the prevention of sickle cell disease (SCD) complications vary in effectiveness and are associated with risks/tolerability issues. PF-04447943, a selective inhibitor of the cyclic guanosine monophosphate−specific phosphodiesterase-9A enzyme, is being developed for prophylactic therapy to reduce the incidence of vaso-occlusive crises in patients with SCD. Herein, we report on the safety and tolerability of PF-04447943, based on a large data set from the clinical trial program.

**Methods:** The PF-04447943 safety database includes data from 8 phase 1 studies in healthy adult and elderly subjects, a phase 2 study in patients with Alzheimer’s disease (AD) from a previous development program, and a phase 1b study in stable SCD patients. Study durations ranged from 1 day to 3 months. Data are presented descriptively.

**Results:** Safety data for 277 patients receiving PF-04447943 were available. In phase 1 studies, 164 subjects received PF-04447943. Frequently reported treatment-emergent adverse events (TEAEs) were headache, diarrhea, and nausea, which were generally mild in severity. In the phase 1 thorough QTc (TQT) study (N=44), at therapeutic and supratherapeutic doses, PF-04447943 was not associated with QTc interval prolongation that met the threshold of clinical concern, based on ICH E14 criteria. In the phase 2 study of the AD development program (PF-04447943, n=91; placebo, n=100), the incidence of TEAEs was 63.7% with PF-04447943 and 58.0% with placebo. Incidence of all-causality AEs in the gastrointestinal disorders class (including abdominal pain, diarrhea, dry mouth, dyspepsia, gastroesophageal reflux disease, intestinal obstruction, nausea, and upper gastrointestinal hemorrhage) was higher with PF-04447943 (19.8%) vs placebo (5.0%); no other notable differences were observed. In the phase 1b study in SCD patients (safety analysis set: PF-04447943, n=22; placebo, n=7), nervous system disorder TEAEs (eg, headache) occurred more frequently with PF-04447943 (25 mg BID, 60%; 5 mg BID, 57%) vs placebo (29%). In total, 6 serious AEs (sickle cell anemia with crisis, n=4; pneumonia, n=1; biliary colic, n=1) occurred in 3 patients receiving PF-04447943; all were consistent with the course of SCD and were not considered to be treatment related.
Conclusion: Review of the safety database for PF-04447943, which includes 267 patients who received the study drug, indicates that PF-04447943 is generally well tolerated, with no major safety signals. Planned long-term, phase 2 and 3 studies of PF-04447943 in patients with SCD will provide additional safety data in this population.
JSCDH-D-17-00043: HBI-002, an oral carbon monoxide therapeutic, is a modulator of vaso-occlusion in transgenic sickle cell mice

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Affiliation: *University of Minnesota, **Hillhurst Biopharmaceuticals, Inc., ***Beth Israel Deaconess Medical Center

Abstract

Background: The literature describes carbon monoxide (CO) as a potential therapeutic agent in sickle cell disease (SCD). Exogenous CO impacts SCD through four distinct mechanisms: (i) limiting the formation of HbS polymers; (ii) up-regulating anti-inflammatory pathways; (iii) promoting anti-oxidant and anti-apoptotic activity; and (iv) causing vasodilation.

CO prevents and reverses HbS polymerization (Sirs,1963; Higgins,2007; Aroutiounian,2001). Further, three studies in four different SCD transgenic mouse models demonstrated that CO (as low as 2% COHb) improved blood flow and decreased cellular inflammatory signals, hepatic necrosis, and mortality (Belcher,2006; Beckman,2009; Belcher,2013).

Reports also show CO clinically to reduce sickling (Sirs,1963) and extend the red cell lifespan in SCD patients (Beutler,1975). Epidemiologic literature suggests that CO might prevent the occurrence of vaso-occlusive crises (Yallop,2007). Safety data have been generated in seven Phase 1 and 2 clinical trials with other forms of CO delivery, one in SCD patients, where CO was shown to be safe and well tolerated (Mahan,2012; Howard,2014; Misra,2014, Bathoorn,2007; Mayr,2004; Rhodes,2009).

HBI-002 is a CO-containing liquid. The bioavailability of CO through oral administration of HBI-002 has been demonstrated in rodents, with peak COHb <10%. Oral administration of HBI-002 is predicted to enable chronic administration of CO without the potential environmental safety and toxicity of other forms of CO.

Methods: Male and female NY1DD transgenic SCD mice were dosed with HBI-002 (n=3;3) or placebo (vehicle, n=3;3) by oral gavage using two dosing regimens. Peak COHb levels were found to be 5%. NY1DD mice with implanted dorsal skin-fold chambers received HBI-002 either (i) daily for three days or (ii) once 24 hours prior to hypoxia. Immediately before hypoxia, 20-25 flowing venules were selected and mapped. Mice were subjected to one hour of hypoxia (7% O2), followed by re-oxygenation in room air. All venules were re-examined for blood flow at 1, 2, 3 and 4 hours after hypoxia. The number of static (no flow) venules were counted and % stasis was calculated.

Results: The percent stasis was significantly lower in HBI-002 treated animals compared to control at all time points with both dosing regimens. The
improvement in degree of stasis was dosing regimen dependent, with degree of stasis lower in animals treated with the longer dosing regimen.

**Conclusion:** These data indicate the efficacy of HBI-002 in this transgenic SCD mouse model and demonstrate that HBI-002 is similarly effective in thwarting SCD pathophysiology in SCD mouse models as reported with other forms of CO delivery.

**POSTER SESSION, SUNDAY, APRIL 30, 2017**

**JSCDH-D-17-00020: Development of a Hydroxyurea Clinical Decision Support Toolkit for Healthcare Providers**

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**Abstract**

**Background:** Compelling evidence shows that hydroxyurea can significantly reduce medical complications and improve the quality of life in patients with sickle cell disease (SCD), however it is highly underutilized. Only 20-30% of eligible adult patients are being prescribed this disease-modifying therapy. Studies have shown that provider knowledge and low comfort level with managing hydroxyurea are important barriers that limit utilization of the medication and infer a need for provider education and clinical support tools.

To address these needs, the Sickle Treatment and Outcomes Research in the Midwest (STORM) regional sickle cell network partnered with providers and patients to co-create a hydroxyurea clinical decision support toolkit.

The goal was to create an innovative intervention with easily accessible tools to improve provider knowledge, self-efficacy and comfort level in prescribing and managing hydroxyurea.

**Methods:** STORM’s Regional Coordinating Center partnered with the Live Well Collaborative (LWC) to develop the hydroxyurea toolkit over a 12-week period that included five phases. During phase 1, semi-structured interviews were conducted with 20 healthcare providers throughout the Midwest, (3 advanced practice nurses, 4 pediatricians, 13 pediatric and adult hematologists). Interview themes were analyzed and mapped to identify
provider needs for managing hydroxyurea. Phase 2 focused on literature searches for clinical decision support tools, and provider educational preferences. During phase 3, the team translated research insights into conceptual ideas. In phase 4, the LWC team tested and refined the project concepts with the STORM network at a regional Learning Session through a co-creation activity that prioritized provider tools and website architecture. The final phase is website testing and refinement.

**Results:** Providers identified three needs for managing hydroxyurea: education, communication and treatment optimization. They wanted clinical support tools to be easy to use, with tailored messages and applications in multiple formats (e.g. print-based, web-based, and via mobile-device).

**Conclusion:** This project used design-thinking methods to develop a provider toolkit with the goal of increasing hydroxyurea uptake for patients with SCD. The process revealed a need for easily accessible clinical decision support tools that support hydroxyurea initiation and management “before,” as well as “during,” and “after” clinic visits. Evaluation and testing of the website and clinical decision support tools will determine its effectiveness in increasing provider comfort level, and willingness to prescribe hydroxyurea consensus development statement on hydroxyurea treatment for sickle cell disease. NIH Consens State Sci Statements. 2008 Feb 27-29;25(1):1-30.

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**JSCDH-D-17-00014: Changes in HU Prescription Level in SCD Severe Patients Lead To Savings In Hospitalization Rate: Results Of A French Pharmacoeconomic Study**

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**Abstract**

**Background:** Hydroxyurea (HU) has proven efficacy in several clinical trials to prevent vaso-occlusive episodes of Sickle cell Disease (SCD), an inherited genetic disease affecting red blood cells. Under the European Orphan drug regulation, specific hydroxyurea titrated dose formulations have been developed for the management of SCD (SIKLOS® 100mg and 1000mg of HU) and obtained marketing authorizations in both pediatric and adult patients suffering from SCD. SIKLOS® was launched in France in late 2012. Since this launch a dramatic increase in HU consumption in the SCD patients has been observed leading to a probable better coverage of the severe patients. The objective of this pharmacoeconomic study was to measure the global health improvement
of this increase in HU intake in the French SCD community regarding the hospitalization rate and the severity of the disease.

**Methods:** Several French National Databases were processed in order to establish cross-comparisons of areas over the years 2011 to 2015 (i.e. yearly number of SCD patients, yearly hospitalizations, databases for HU consumption).

**Results:** The whole number of SCD patients in France is estimated between 16,000 and 18,800 (respectively in 2011 and 2015). Using the hospitalization database and to define the severe patient population, the following criteria were used: Patient Hospitalized (at least one night) during the same year at least 3 times and/or a cumulative hospital stay of at least 10 days and/or at least 10 transfusion sessions related to sickle cell disease. In 2011, a total of 2,086 patients met these criteria of severity representing 17.8% of SCD population (Respectively 2,491 and 17.9% in 2015) Comparing the 2 periods, a decrease of the hospitalization rate was observed in the whole severe SCD community (-4.5% of at-least one night hospitalizations). In order to gauge if this decrease is the consequence of the penetration of Siklos®, 3 areas were individualized regarding the increase of HU consumption per SCD capita between 2011 and 2015 (Zone A: no increase in use, Zone B: intermediate increase, Zone C: high increase). The number of hospitalizations increase in Zone A (+10.2%) and decrease in the other areas -13.7% (B) and -4.0% (C).

**Discussion:** The decrease in hospitalization rate (in admission and/or duration: -60 to -80%) of HU in SCD is well described in the clinical trials. In this pharmaco-economic study, this activity is measured in the whole population, showing significant impact of the prescription of the drug in the community.

**JSCDH-D-17-00028:** *Personal Life Goals and Health-Related Quality of Life of Adults after an Allogeneic Hematopoietic Stem Cell Transplantation for Sickle Cell Disease*

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**Abstract**

Hematopoietic Stem Cell Transplantation for Sickle Cell Disease

**Background:** Despite treatment advances, sickle cell disease (SCD) has devastating short- and long-term effects on adults' personal life goals and health-related quality of life (HRQoL). Reduced intensity allogeneic hematopoietic stem cell transplantation (AlloHSCT) from an HLA-matched sibling donor offers adults a
unique therapy to reverse their SCD. The purpose of this analysis was to explore the personal life goals (e.g., employment, school attendance and/or completion, pursuit of a career) and assess their relationship to HRQoL scores among recipients of an AlloHSCT.

Methods: This mixed methods study was conducted with eligible recipients of an AlloHSCT at a large Midwest hospital. Over 2 hours, participants filled out a 6-item demographic form, the HRQoL survey (SF-36, version1) and participated in a 60-90-minute audio-recorded interview (face-to-face or telephone). Verbatim transcripts were processed using MAXQDA qualitative software. HRQoL total and subscale scores were calculated and compared to personal goals identified through thematic analysis.

Results: Eleven of 15 eligible AlloHSCT recipients (75%; 6 female/5 male) participated in this study. Age at transplant ranged from 16-51 yrs ($M = 26.7$) and years since transplant ranged from 1.01-4.11 yrs ($M = 2.71$; $SD = 1.03$). Nine described their transplant as successful and discussed pursuing personal goals including employment, attending college or volunteering. Five indicated that pre-transplant pain and complications interfered with their aspirations, but described being able to pursue their goals more readily. While the HRQoL total scores varied widely (27.27-91.81), the five highest scores (79.44-91.81) were among those able to pursue their personal goals. Four participants with avascular necrosis of the hip or ankle had lower total HRQoL scores (48.57-67.22) reflecting lower subscales. The two participants who identified their AlloHSCT as unsuccessful had low total HRQoL scores (27.78 and 49.86) and described how SCD continued to affect and interfere with their ability to pursue personal goals.

Conclusion: This study shows that health-related quality of life varies among recipients of an AlloHSCT and captures aspects related to the pursuit of personal life goals after an AlloHSCT. However, even after a successful AlloHSCT, a subset with avascular necrosis had functional limitations and lower HRQoL scores. Assessing health-related quality of life and personal life goals is an important aspect of the overall transplant experience. Future AlloHSCT research should investigate the complex relationships among physical and mental health and document how these are intertwined and change over the life course.

JSCDH-D-17-00032: Impacting Sickle Cell readmission in a Pediatric Setting

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Abstract

Background: Sickle Cell disease (SCD) is an inherited blood disorder of the hemoglobin beta-globin protein in the red blood cells which results in significant risk for hospitalization. Since over 100,000 people in the United States have SCD and recurrent hospitalizations occur; this constitutes a significant disease burden that are not
only costly, but also contribute to loss of income, learned helplessness, additional immense morbidities and psychosocial stressors.

Readmission within 30 days after hospitalization for SCD crises was developed at the National Association of Children’s Hospitals (NACHRI) as a measurable benchmark to improve hospital quality. The NACHRI, multi state study of SCD care utilization found an overall readmission rate of 33.4% with lower rates in children (12.8% in children age 1-9 and 23.4% for patients ages 10-17)

**Methods:**
- Nurse coordinator
- Standardize teaching on SCD via direct interactions with caregivers & patients
- Sickle Cell Action Plan
- Increase rate of parental/patient consent for hydroxyurea
- Increase influenza immunization rates (influenza) to greater than 85%
- Nursing discharge call backs at 24hr & 72hr after discharge

**Results:** Reviewed admission/readmissions for SCD patients in 2014 and 2015; 52% females/48% males.

Pre-intervention in 2014 there were 91 sickle cell related admissions with 14 re-admissions. Following implementation of the interventions in 2015, there were not only 59% fewer admissions (63), but also 58% fewer readmissions (6 re admit/63 discharges). The interventions affected both admission rate and readmission rates.

**Conclusions:** SCD hospitalization rates continue to pose a major challenge. Although there is undoubtedly much room for additional progress in this area, we have made a start towards improving our sickle cell population’s health.

**Sickle Cell Action Plan for:**
### GREEN ZONE (No pain) This is where you should be everyday.

**Things to Do Every day:**
- Drink 4 drinks every day to stay hydrated
- Be aware of Sickle Cell Triggers: Cold, Illness, Change in Weather
- Make sure you are up to date on your Sickle Cell Well Care
- Take medications daily:

### YELLOW ZONE (Having mild pain)

- Drink extra fluids daily
- Use heating pads for comfort to painful areas
- Take Ibuprofen - by mouth every 6 hours
- Take temperature before each dose of Ibuprofen and go immediately to RED ZONE if temperature is 101 or greater
- Use 4 tablets by mouth every 6 hours for pain not relieved by ibuprofen
- If pain is not improved in 24 hours, go to the RED ZONE and call your Pediatric Hematologist

### RED ZONE (STOP AND CALL PEDIATRIC HEMATOLOGIST)

I’m in the RED ZONE if:
- Pain is not improving after 24-48 hours
- Fever (temperature 101 or greater)
- Unable to control pain at home
- Unable to drink well, having diarrhea/vomiting
- Chest pain, Shortness of Breath
- Abdominal pain
- Severe fatigue
- Not acting like yourself

*If an emergency, call 911 or go to nearest Emergency Room*

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**Baseline Hemoglobin:**

**History of Acute Chest Syndrome: Last Transfusion: Last Admission:**

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**JSCDH-D-17-00010: Navigating the Health Care System: Challenges and Successes of Sickle Cell Transition Workshop**
Purpose: To create an educational program to provide information and resources to assist adolescents with Sickle Cell disease transition to adult care. The goal of the transition workshop was to provide the patients with the necessary skills and knowledge needed to navigate the adult medical system.

Background: Health care transition is the process of changing from a pediatric to an adult model of health care (National Health Care Transition Center). The goal of a planned health care transition is to maximize lifelong functioning and well-being for all youth, including those who have special health care needs and those who do not (AAP). One of the challenges of transitioning to adult care is the lack of parental guidance and the overwhelming responsibility of their disease management. Adolescents lack the skills necessary to navigate the healthcare system.

In response to the barriers to transitioning from pediatric care to adult and the concerns expressed in our transition clinic; a transition workshop was developed to further educate and prepare this population for the adult healthcare system. The goal of the workshop was to focus on five key areas in the transition process: medical care, educational and vocational issues, healthcare benefits, psychological health and social well-being. During the transition workshop, patients learned to take an increasingly active role in their own medical care. They also had the opportunity to visit adult hospital and speak with an adult hematologist, nurses, and administrative personnel. The main challenge of the transition workshop was enrollment and participation in the workshop. Despite the challenges, the workshop was a success as many patients gained confidence in the ability to navigate the adult healthcare system.

Conclusion: This transition workshop experience provided the collaborative group between the adult and pediatric Hematology service providers in Delaware. As a result of this workshop the patients were empowered to be their own health advocates through skill-based learning.
Abstract

With the increasing trend of clinical care of patients with SCD in the community, it is imperative that educational programs address the need. The NMA held a Professional Development Series at the Congressional Black Caucus Foundation, Inc’s 46th Annual Legislative Conference on September 14, 2016 at the Walter E. Washington Convention Center in Washington, DC. This one day educational activity included a panel entitled, Sickle Cell Disease – What Every Physician Should Know, led by Dr. Edith Mitchell and featured Drs. Wally R. Smith, Krupa Sivamurthy, and Biree Andermariam as presenters.

Methods: Prior to the activity participants were surveyed using a Likert Scale regarding their perceived ability to describe the spectrum of sickle cell disease and its management parameters including pathophysiology, genetics, diagnosis, and best practices for the pediatric to adult transition. Survey response choices ranged from 1 to 5, with 5 indicating strong agreement with being able to perform the objective and 1 indicating strong disagreement with being able to perform the objective.

Results: The following summarize the respondents’ perceived ability to perform the stated objective prior to the learning activity:

- 20.51% indicated a Strong Agreement
- 35.90% indicated Agreement
- 23.08% indicated Not Certain
- 15.38% indicated Disagreement
- 5.13% indicated Strong Disagreement

For an average weighted score of 3.51 or “Not Certain”. Post activity participants were again surveyed using the same Likert Scale. The following results summarize the respondents’ perceived ability to perform the stated objective post learning activity:

- 61.90% indicated a Strong Agreement
- 33.33% indicated Agreement
- 4.76% indicated Not Certain
- 0% indicated Disagreement
- 0% indicated Strong Disagreement.

For an average weighted score of 4.57 post activity. The change in pre verses post activity evaluation results indicates a significant improvement in participant perceived ability to describe the spectrum of sickle cell disease and its management parameters including pathophysiology, genetics, diagnosis, and best practices for the pediatric to adult transition. Additional educational programs are needed to enable community and minority providers the resources to bring therapies to SCD patients that extend and significantly improve their lives.
JSCDH-D-17-00022: The Impact of Sickle Cell Disease in Children on Health Care Costs in Indiana

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Abstract

Background: The health care costs associated with prevention of and treatment for complications due to the pathophysiology of sickled red blood cells remain poorly elucidated. The cost-of-care studies executed to date are very few, but reveal some important statistical data for this chronic disease. The objective of this study was to provide much-needed epidemiological data to clarify the current economic burden of health care costs for patients with sickle cell disease in central Indiana.

Methods: We obtained Institutional Review Board approval to conduct this study via data extraction based on ICD-9-CM and ICD-10-CM codes specific to sickle cell. Individuals ≤21 years of age with sickle cell disease treated at any Indiana University Health facility from 7/1/11 to 6/30/16 were eligible for inclusion. The unit of analysis was the patient encounter.

Results: In this 5-year period, 428 unique patient encounters were identified, for which $4,024,929 in health care costs were incurred. Highlights of baseline demographics and clinical characteristics reveal that the most prevalent sickle cell disease genotype was hemoglobin SS (55%), the predominant race and ethnicity were respectively Black (97%) and non-Hispanic (98%), the cohort was 56% male, and the principal payer source was public insurance (74%). Health care costs consisted of two types of health care services, namely inpatient (hospitalizations) and outpatient (clinic) encounters. Total inpatient care represented 57% of all services but accounted for 63% of all charges with an average encounter cost of $5200/year; in contrast, total outpatient care represented 43% of all services but accounted for 37% of all charges with an average encounter cost of $900/year.

Conclusions: The study analysis confirms that the majority of health care expenditures for sickle cell disease in central Indiana occurred in the inpatient setting. There seems to be an upward trend in inpatient costs with age, consistent with Kauf et al and the worsening condition of patients with age given the pathophysiology of sickle cell. The findings suggest that reduced hospitalizations would ease the economic burden for sickle cell. This is especially important since the principal payer source for health care in this cohort is public, which parallels the findings in the national statistical brief spanning from 1994 to 2004. To accomplish this goal, we suggest that policy makers implement comprehensive education for providers and patients as well as support preventive and curative therapies in the outpatient setting.
Acknowledgements: We greatly appreciate the funding support from the Community Health Engagement Program of the Indiana Clinical Translational Sciences Institute as well as the hard work by Donna Kelsey-Maddux from University Pediatric Associates for assistance with data extraction based on ICD-9-CM and ICD-10-CM codes specific to sickle cell.

JSCDH-D-17-00035: The Use and Effectiveness of Traditional Medicine for pain management in sickle cell patients in Ghana

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Abstract

Background: Sickle Cell Disease (SCD), a common genetic disorder characterized by the sickling of red blood cells, carries a significant public health burden in Ghana. Recurrent, disabling pain, often leading to organ failure and death in childhood and early adulthood, is the hallmark of SCD. Despite the widespread use of narcotic analgesics, pain is not adequately controlled with conventional treatment in SCD, leading individuals to resort to other methods of pain control. Although traditional medicine is an integral component of the Ghanaian health care system, there is little information about the use of traditional medicine to treat pain crisis in SCD patients.

Objective: To survey the extent and effectiveness of traditional medicine use for pain control among adult patients with SCD.

Methods: 178 adult SCD patients were enrolled in the study, from 2013 to 2015, at the Korle Bu Teaching Hospital Center for Clinical Genetics in Accra, Ghana. A cross-sectional prospective cohort study design was used for this sub-study. The severe genotype (SS/S-Beta Zero Thal) was represented by 64.1% (n=114) and the mild genotype (SC/S-Beta Plus Thal) by 33.2% (n=59). In-person comprehensive questionnaires were administered to patients. The questionnaires focused on demographics, medical history, family medical history, education, and lifestyle choices, which include questions on traditional medicine. All adults who were obtaining treatment for SCD at the clinic were invited to voluntarily...
complete the questionnaire.

**Results:** Of the 178 respondents who completed the questionnaire, 54 (30.3%) indicated that they have used traditional or complementary medicine in the past. The frequency of traditional medicine used was higher among females (57%), adults age 25-34 (40.7%), those with a high school or college level of education (74.1%), and those with Sickle Cell Anemia (SS) (48%). A significant portion of participants (43.9%) reported using traditional medicine for pain control, of which, (41.5%) said it was effective in decreasing their level of pain. When questioned about whether they had informed their treating physician of traditional medicine use for pain, 38.9% responded that they had, although 50% reported they believed it was important to do so.

**Conclusions:** Our study showed traditional medicine use is common among adult patients with SCD. However, further well-designed prospective studies are needed to investigate the use of the different types of traditional medicine for pain in SCD. Furthermore, a clearer understanding of the patterns and causes of traditional medicine use will have a positive impact on the quality of care physicians can offer their patients.
JSCDH-D-17-00050: Understanding the Self-Management Practices of Young Adults with Sickle Cell Disease

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Abstract
Because self-management is central to sickle cell disease (SCD) management, this descriptive study of 18 young adults with SCD, ages 19-39, was conducted to understand their pain experience and to identify the specific home activities they use for pain prevention and management prior to care-seeking. Participants completed two baseline surveys and one semi-structured, individual interview. Content analysis of the interview transcripts yielded two themes: difficulty in describing pain and living with pain. Participants used pharmacological and non-pharmacological strategies to alleviate pain and avoid disease complications but report barriers to using these strategies. Healthcare providers should use study findings to provide appropriate care to and improve pain outcomes for young adults with SCD. In addition, interventions aimed at addressing barriers and optimizing self-management are needed.

Understanding the Self-Management Practices of Young Adults with Sickle Cell Disease

Sickle cell disease is a genetic condition involving pain syndromes, infections, organ damage, and other disease complications (1,2). The survival of individuals with sickle cell disease (SCD) to age 20 was 50% in the 1940s (3). Today, 50% of individuals with SCD live past age 50. Although SCD mortality has decreased, the disease experience is still predominantly characterized by debilitating pain, especially among young adults (1). Self-management is a daily, self-motivated, and collaborative process (involving patients, their family members, and healthcare providers) to manage symptoms in chronic disease (4). Self-management is vital to daily management and prevention of SCD pain; thus, it is necessary for successfully living with the disease (5).

In recent years, self-management has been increasingly studied in chronic pain conditions, such as rheumatoid arthritis and multiple sclerosis, but it has been less frequently evaluated in individuals living with SCD (6,7). One
might inaccurately assume that self-management is universal. In fact, self-management has been conceptualized in different ways in various chronic conditions and care needs vary across conditions wherein individuals experience pain (8). Unique aspects of SCD make self-management different and, some would suggest, more important than in other conditions. Sickle cell disease is a chronic, progressive condition (1,2). Without a viable cure for all affected, disease management involves pain medications, Hydroxyurea (Hydrea®; reduces levels of abnormal hemoglobin), and red blood cell transfusions (9-14). Pain management is often reported by individuals with SCD as inadequate or ineffective, and healthcare utilization is frequently associated with discrimination and accusations of drug-seeking (15-18). Consequently, individuals with SCD often avoid the healthcare system. Because they experience most of their pain at home, disease management is heavily dependent on self-management (19). Individuals use home self-management to manage pain until it is no longer effective, and then healthcare is sought (15). Young adults with SCD are particularly at risk for poor or inadequate management of pain because they are in transition from pediatric to adult care, face increased responsibility for self-management, experience frequent pain episodes and high healthcare utilization, and must deal with increased risk for health-related stigmatization (20-23).

Self-management in SCD is primarily focused on managing pain and preventing disease complications (24). Health recommendations for living well with SCD include getting good medical care and regular checkups, preventing infections, and learning healthy habits (25). Middle-aged and older adults with SCD most frequently attribute living beyond expectations to learning how to care for themselves (26). They recommend self-management activities such as gaining knowledge and understanding of SCD, listening to and learning about the body, praying, following providers’ orders, hydrating, resting, eating good food, and avoiding drinking, smoking, and using drugs (27). They also use emotional support, physical activity, and complementary and alternative medicine (28). Similarly, young and middle-aged adults with SCD control symptoms with preventive action including dressing and preparing for the weather, keeping painkillers at home, monitoring diet, avoiding alcohol and partying, limiting activities, and resting (29).

We know that SCD symptomatology varies according to each individual, even those with the same disease type; however, we believe that young adults experience patterns of pain and utilize specific self-care behaviors. These patterns and behaviors have not been fully evaluated in previous studies. A thorough evaluation will contribute to a better understanding of self-management, help in identifying care requirements for young adults, and serve as a starting point in developing interventions for improving self-management in this population. Therefore, the purpose of this study was to obtain a better understanding of the pain experience of young adults with SCD and to assess home self-management practices used to prevent pain crises and manage pain prior to care-seeking.
Methods: Nola Pender’s Health Promotion Model (HPM) is used to understand the multi-dimensional nature of health behaviors (30). The HPM identifies three groups of factors which influence health behaviors: individual characteristics and experiences, behavior-specific cognitions and affect, and behavioral outcome. The theory suggests that personal, interpersonal, and environmental factors positively or negatively influence beliefs and the practice of health-promoting behavior. Self-management practices of young adults with SCD can be elucidated using the HPM because beliefs regarding SCD and the symptom experience can affect performance of self-management. In this study, we focused on prior SCD symptom experience, perceived benefits of self-management, perceived barriers to performing self-management, perceived self-care ability, and immediate competing demands and preferences.

This was a qualitative, descriptive study involving surveys and individual interviews. Surveys provided demographic data and a baseline self-management assessment. Interviews provided more detail about quantitative findings related to participants’ pain experience and home pain management. Participants were 18 Black adults with a SCD diagnosis, ages 19-39, who were recruited from an outpatient sickle cell clinic. There were no exclusions based on education or socioeconomic status.

Before study commencement, Institutional Review Board approval was obtained from the university associated with the SCD clinic. Purposive sampling was then used to enroll participants between February and March 2014. Prior to the weekly clinic day, the first author reviewed the appointment schedule to identify patients meeting the inclusion criteria and collaborated with clinic staff to exclude individuals with known cognitive impairment. During the clinic day, she approached potential participants in a private area of the clinic, described the study, and sought participation. After all questions were answered, individuals provided written informed consent and completed two baseline questionnaires. Participants were then invited to complete an in-person or telephone interview at a date and time most convenient for them. Interviews, averaging approximately 30 minutes, were audio-recorded, professionally transcribed verbatim, and checked for accuracy by the first author. Total study participation time did not exceed 60 minutes. Each participant received $30 for completing the questionnaires and the interview.

Data were collected using the following instruments. The demographics and health history form was used to gather data regarding items such as age, gender, race, ethnicity, SCD type, annual income, years of education, number of annual pain crises, number of crises managed at home, and daily pain rating. The Appraisal of Self-Care Agency Scale (ASA) is a 24-item scale that was used to measure perceived self-care ability; the perceived ability to participate in general therapeutic behaviors to enhance and/or maintain health status and quality of life (31). Items are scored on a scale of 1 to 5 (“totally disagree” to “totally agree”) and higher total scores (maximum of 120) correspond with higher levels of perceived self-care ability. The
Jenerette Self-Care Assessment Tool (JSAT) is an eight item scale that was used to measure self-care actions; one’s participation in SCD-specific therapeutic activities and using resources to enhance health status and quality of life (31). Items are scored on a scale of 1 to 4 (“never” to “almost always”) and higher total scores (maximum of 32) indicate higher self-care actions. Participants’ medical records were reviewed to confirm SCD type and to assess items such as past medical and surgical history, laboratory values, and current medications. The first author developed a semi-structured interview guide that she used to conduct the individual interviews. A sample item was “Tell me about the things that you do to live with your sickle cell disease”. Participants' responses guided thematic exploration and probing was used to obtain details.

Statistical Package for the Social Sciences (SPSS, Version 22) was used to calculate descriptive statistics from the demographic and scale data, while interview data were subjected to content analysis (32). As interviews were conducted, the first author completed an initial review of the first seven transcripts to identify themes based on emerging concepts and developed an analysis coding sheet (33). Subsequently, both authors independently analyzed all transcripts using the coding sheet. Independent findings were compared (there were no disagreements) and consolidated.

Scientific rigor, data validity, and quality assurance were maintained throughout the study. During data collection, respondents clarified interview statements and validated the interviewer’s understanding of the data (34, 35). The second author has over 20 years of research expertise in self-management and SCD. During data analysis, coding was reviewed by both authors and frequent consultations occurred to achieve agreement regarding themes and interpretations.

Results: The sample of 18 individuals, ages 19-39, were mainly African American (n = 17; 94%) females (n = 10; 56%) with the most severe form of SCD - sickle cell anemia (n = 15; 83%) (Table 1). Their mean age was 26.7 years (standard deviation = SD 5.8) with 13.2 average years of education (SD 2.2). Participants used numerical ranges to describe their pain experience. The majority reported average daily pain of 7-10 (n = 10; 56%) on a scale from 0-10, with 0 being no pain. Most people reported experiencing 2-7 pain crises annually (n = 10; 56%). Of those who experienced 20 or more crises annually (n=5; 28%), 60% belonged to the 19-25 age group and 60% were female. Approximately 4-8 crises were managed at home (n = 8; 44%) while 1-3 crises required emergency department visits (n = 8; 44%) and hospital admissions (n = 10; 56%) (Table 2). Participants experienced various comorbidities and SCD complications with acute chest syndrome (n = 15; 83%) being the most common. Hemoglobin levels ranged from 6.3 G/DL – 14.6 G/DL and the most frequently prescribed medication was folic acid (n = 18; 100%) (Table 3). Perceived self-care ability scores (ASA) ranged from 73 to 100; average of 86.33. Self-care action scores (JSAT) ranged from 25 to 32; average of 29.11.

Participants’ responses to interview questions are presented using two themes: 1) Pain is difficult to describe and 2) Living with pain. Table 4 provides demographic data for
participants whose thematic exemplars are included here. Their names have been changed to pseudonyms.

Pain is Difficult to Describe
When asked to describe their pain, participants reported mild to severe (1 to 10+) pain which occurred infrequently to daily. This pain was both unpredictable (“good one minute and then pain the next minute”) and predictable (“know something you did done messed you up”). Some individuals experienced regular pain, described as different from a crisis pain, while a few reported any pain as a crisis. When asked to define a pain crisis, participants provided physical and physiological/medical descriptions. Neil and Jacob (respectively) provided examples of these descriptions: "Like an extreme pain that...you have no control over and like it lasts for a long period of time...It would get worse from there." "...I would probably explain it like I don’t have enough...oxygen flowing through my blood cell and my cells turn into a sickle."

Participants used descriptive terms including aching, sharp, stabbing, throbbing, constant, dull, intermittent, shooting, gnawing, excruciating, and unbearable. However, they discussed the difficulty often faced in attempting to describe their pain experience using descriptors. Some described their pain as simply: “bad”, “no comparison”, “normal to have pain”, “pain is a crisis”, “it is what it sounds like”. Carla and Rachel (respectively) stated: "I’ve never been able to explain to somebody the type of pain. It’s just the worst pain you can think of.” "...I can’t really describe the pain. Cause it's, it's not like a stabbing. I don’t know. It’s just a constant pain in your joints. I mean, it could be anywhere basically but each pain is different. So, it’s not one pain that’s the same....it is a constant pain though."

Among young adults with SCD, pain is prevalent. Although this pain may be categorized, young adults find it challenging to describe their pain experience.

Living with Pain
Participants used a variety of strategies to live with (manage and prevent) pain. They stated that although nothing makes a pain crisis “easier”, some things “help”. Prior to care-seeking, two major types of self-management practices were used in combination: pharmacological and non-pharmacological methods. Pharmacological aids included pain medications to manage pain and “sickle cell medications” such as Hydroxyurea to prevent pain or decrease pain frequency. To avoid and/or deal with pain, participants used a variety of non-pharmacological methods including hydration; distraction; warmth/heat via heating pad, electric blanket, and/or hot shower; and staying active. Distraction included visiting with friends and family, watching television, listening to music, dancing, reading novels, doing outdoor activities, and using humor. Complementary and alternative techniques included spirituality (prayer and reading the Bible), breathing exercises, massage, meditation, and relaxation. Strategies used most often included pain medications, hydration, SCD medications, and distraction. When asked about the most important things they do to care for themselves, participants reported: drinking water often, consistently taking medications, keeping up with doctor’s/clinic

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appointments, limiting stress, staying in good spirits/staying positive, and staying active.

Individuals who experienced an average of 2-7 pain crises annually used more self-management strategies than those who experienced more pain crises. Individuals in this group most commonly used hydration, pain medications, SCD medications, distraction, and staying active. Only these individuals reported using meditation, oxygen, rest, breathing exercises, massage, and avoiding stress. Females used more self-management practices than males and they most commonly used hydration, pain medications, SCD medications, and distraction. Participants in the 19-25 age group used more self-management strategies than individuals in other age groups. They most commonly used hydration, pain medications, SCD medications, and distraction.

In response to being asked “what makes it easier to perform self-care behaviors”, participants reported a desire to not be in pain and avoid complications, social support, setting priorities, and faith. For the majority of the participants, 1-3 people live in their household; this provides insight into social support. Self-care strategies most commonly used by these individuals included pain medications, hydration, and SCD medications. The two participants who lived alone had one self-care strategy in common – taking pain medications and only one of the two reported hydration as a strategy.

When asked “what makes it harder to perform self-care behaviors”, participants reported things such as everyday life/daily responsibilities, work, stress, pain, and school. They noted similar barriers to performing self-care behaviors despite the average number of pain crises experienced annually. However, pain was reported as a barrier only by those who experienced an average of 2-7 pain crises. Everyday life/daily responsibilities included caring for family, household tasks, and “things that I have to do”. Frank explained: “Let’s see, everyday life. You know sometimes like some people have jobs where they can't just stop and do the things they need to do. Or some people have jobs that just isn’t good for people with sickle cell. That's the job they have and there’s nothing they can really do about it...But just everyday life. It all depends on people’s lives. If you have kids, you'll never get that time to sit, rest, take some deep breaths. You know actually, cause running around and staying busy and not ever settling down and giving your body time to rest so you into a crisis over time too and those usually the worse.”

Young adults with SCD employ a set of self-management strategies to manage and prevent pain prior to care-seeking. However, they encounter barriers to using these strategies.

Discussion:
This study adds to the limited body of knowledge regarding self-management in SCD and sheds light on self-management practices young adults use to prevent and manage pain prior to care-seeking. Although the SCD pain experience is individualized, a range of pain patterns and self-management practices were identified. A pain crisis was primarily described using sensory qualities of pain. Like individuals with
cancer, participants used descriptive terms associated with somatic (such as aching and sharp), neuropathic (such as stabbing and shooting), and visceral (such as constant and dull) inferred pain mechanisms (36). Use of these terms is important for pain management because types of pain are treated differently. For example, somatic pain may be treated with anti-inflammatories while neuropathic pain may be more responsive to anticonvulsants (36).

Young adults with SCD experience difficulty in describing their pain. Pain is subjective, but participants' use of responses such as “bad”, “normal to have pain”, and “it is what it sounds like”, when not in pain, makes it easier to understand their difficulty in communicating pain intensity to healthcare providers beyond the numerical scale. Interestingly, participants did not use numerical descriptors unless specifically asked. Perhaps these descriptors are not as meaningful to individuals with SCD. Moreover, the difficulty experienced with using descriptors, such as continuous, throbbing, and stabbing, is problematic because these are examples of terms commonly used by healthcare providers during pain assessments. Current assessment methods may need to be redesigned to better capture the total patient experience to more effectively address pain. Participants also emphasized that living with SCD “is not as easy as people think” and that unfortunately, healthcare providers still need to be educated about the disease. This makes it difficult for individuals to get care. Along with recently published SCD care guidelines, Matthie, Jenerette, and colleagues offer information that can help to fill the knowledge gap for providers (37-39). Notably, the psychosocial aspects of living with chronic and acute pain, and care-seeking while being at risk for health-related stigmatization, still need to be addressed for this vulnerable, minority population.

Study participants indicated a desire to engage in self-management to optimize health, and they used a combination of strategies consistent with previous recommendations and reports from middle-aged and older adults with SCD (25, 28, 40). Behaviors most helpful in managing pain were staying hydrated and taking medications daily but everyday life sometimes “got in the way”. This supports previous reports as to why young adults with SCD delay care-seeking – because of competing time demands related to family, school, and work (15).

There is an ongoing challenge to maximize self-care ability and actions in individuals with SCD. Participants' responses to the ASA items indicate that they have the ability to care for themselves and in fact, know what to do for the best health outcomes. However, responses to the items on the JSAT, which actually measures self-care actions, indicate that young adults with SCD often choose not to participate in self-management activities such as avoiding stress and adhering to a recommended diet. Approximately 10 years ago, Jenerette and Murdaugh (31) reported an average ASA score of 87.85 and a JSAT score of 28.22 in adults with SCD. These are similar to the current average scores; ASA of 86.33 and JSAT of 29.11. Interview responses explain the common gap between ability and action in young adults. These individuals are perhaps still "learning
their bodies” but they have a good idea about the things they need to do to care for themselves. Despite this knowledge, they choose to do other things because they have similar life challenges of others such as school, work, and family. Results suggest that some young adults may not be equipped to make needed life adjustments for successfully aging with SCD.

These young adults with SCD report everyday life/daily responsibilities and work as the most frequent barriers to self-management. In previous research, middle-aged and older adults with SCD report major life satisfactions as family, employment/education, and religious activities (26). Similarly, many young adults with SCD report employment, education, and family as everyday life activities and daily responsibilities. Self-management may be enhanced by decreasing or eliminating barriers. For example, individuals with SCD should be mindful about employment. Jobs involving significant manual labor can lead to negative health consequences. Education can lead to better employment opportunities, but to move toward educational goals, individuals with SCD should access available resources in educational settings.

Another significant area of risk for young adults with SCD is delayed care-seeking. Care-seeking is included in appropriate self-management. Older and middle-aged adults with SCD emphasize the importance of receiving medical care from knowledgeable providers (26, 27). However, care-seeking is often delayed by young adults due to their perspectives on the importance of time in their lives. Although they are living with SCD, they have similar life activities and responsibilities of their peers and may choose not to forego them. In fact, Jenerette, Brewer, & Ataga (15) report examples of young adults delaying or avoiding care-seeking because of work, school, or the potential to disrupt planned family activities. Certainly, other young adults make similar choices, but the consequences can be quite different for individuals with SCD.

Results support the usefulness of Pender’s model in understanding self-care ability, behavior challenges, and choices of young adults with SCD. The symptom experiences of each individual with SCD differ although they often share the hallmark symptom of pain. Young adults’ pain responses are significantly influenced by personal, interpersonal, and environmental factors. For instance, young adults try to keep up with everyday life and daily responsibilities, often at the expense of self-management. This contrasts older adults with SCD who are more likely to prioritize self-management to promote health (26, 27, 40). Young adults with SCD may be taking risks by not completing known self-management activities because of the health-related stigma attached to SCD that affects every aspect of their lives and is most evident during the transition from pediatric to adult care (23).

This study is important to understanding self-management in young adults with SCD. Findings suggest that young adults need assistance in balancing self-management and daily life. In addition, there is an important contrast between self-m
management practices of young adults and middle-aged/older adults with SCD.

Implications for Research and Practice: This study offers findings necessary for providing appropriate care to and improving health outcomes for young adults with SCD. Findings suggest the importance of assessing facilitators of and barriers to self-management in each individual with SCD, and developing patient-centered, interdisciplinary plans of care. Healthcare providers must get to know members of this population. They must identify young adults’ needs and understand self-management practices used. Needs assessments must include ways to characterize individuals’ pain experiences and patterns while also helping them to learn their bodies and best understand how to apply their self-management abilities to optimize self-management practices. Healthcare providers need to fully assess self-management ability and practices. Moreover, it is important for providers to go beyond treating physiological symptoms of pain and understand the substantial psychosocial issues influencing self-management among young adults with SCD.

References


Our research supports the need for additional self-management studies of young adults with SCD; namely studies involving measurement of self-management activities and development of interventions for increasing the ability to perform these activities. Self-management interventions incorporating educational and skill-building components need to be culturally tailored and tested to meet the needs of young adults with SCD. The wisdom and experiences of middle-aged/older adults can be used to help design these interventions for young adults to move them toward optimal self-management earlier in life. Tailored interventions may need to be different for females and males living with SCD. In future studies, these self-management interventions should be developed. With appropriate measurement and intervention, young adults may be better equipped to deal with the challenges of SCD while successfully aging.


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