MANAGEMENT OF PAIN FROM SICKLE CELL DISEASE

Pediatric Pain PRN Curriculum

Ann & Robert H. Lurie Children's Hospital of Chicago

The MAYDAY Fund

Table of Contents

Objectives

- Apply a multimodal approach to care for children experiencing pain from Sickle Cell Disease (SCD)
- Describe age-specific pain assessment practices, diagnostic tools, and treatment strategies for pain related to SCD
- Involve the patient, family and interdisciplinary care team in the management of pain from SCD

Sickle Cell Disease

Christopher

What questions would you ask Christopher when collecting his medical history?

Christopher is a 15-year-old with SCD-SS. Record of his first vaso-occlusive pain crisis was at 9 months when he presented with dactylitis. Since then he has had painful episodes of various types treated by his hematologists with periodic consultations with pain management specialists.

Christopher arrives in the ED accompanied by his mom.

Dactylitis

- Painful swelling of the hands and feet
- One of the first complications in sickle cell syndromes
- Highest incidence from 6 months to 2 years of age
- Treatment is fluids and pain medication
- Typically resolved in a few days without sequelae

Christopher

What are your first impressions?

Which pain assessment strategies or approaches would you use?

His mom states she has to go to work and can not stay .

Christopher looks younger than his reported age of 15 years. He is "glassy eyed" with yellow tinged sclerae, and dark circles under his eyes.

Vital Signs: HR 100, BP 140/86, RR 24 T 37

- *Pain Location: Headache & both legs and lower back*
- *Pain Intensity: "12" on a 0-10 scale*
- *Pain Quality: "Like I need to be in the hospital" Constant*
- *Aggravating Factors: "Moving, walking"*
- *Alleviating Factors: "nothing"*

Sickle Cell Disease

Sickle cell disease (SCD) refers to several related disorders that vary in their clinical symptomatology and genetics.

- SCD is an inherited, autosomal, recessive disorder where hemoglobin has an amino acid change (Glutamate →Valine) in the β globin chain resulting in polymerization, causing the red blood cells to assume a sickled shape.
- Sickle cell anemia properly refers to individuals who are homozygous for the sickle globin gene.
- Individuals heterozygous for hemoglobin S and beta thalassemia trait have a mild sickling disorder termed sickle thalassemia.

Sickle Cell Disease: Significance

The numbers

In the US, the disease affects:

- 100,000 people
- 1:500 African Americans
- 1:1,000-1,400 Hispanic Americans

Sickle cell disease (SCD) is the most common inherited disorder with millions of people worldwide suffering from this disease. Acute pain is the hallmark and most frequent reason for hospitalization of children with SCD.

Yearly medical costs in the U.S. for those with SCD are >$500 million dollars. This far surpasses the costs for other chronic diseases such as asthma, and congestive heart failure.

Standard medical therapy alone has not been effective in reducing pain burden or costs in this population, indicating the need for innovative treatment paradigms.

Pain statistics

Pain experience and life expectancy is variable:

- 5-10% asymptomatic
- 10-20% seriously affected
- Tremendous resilience, strength, and courage required on the part of patients and families to secure appropriate pain management despite racial, ethnic, disease and healthcare bias
- Median life-expectancy is in the range of 40-50 years, but likely normal for many individuals.

Increased frequency and severity of pain episodes are associated with early mortality.

SCD: Significance

Lifespan

In 1973, the average lifespan of a person with SCD in the US was 14 years. Today this average life span has increased to 40-50 years. Advances in diagnosis and care have made this improvement possible.

- Prophylaxis with penicillin starts at or before 4 months of age.
- Screening for an enlarged spleen.
- Transcranial Doppler testing to evaluate blood flow to the brain.
- Treatment with chronic transfusion for those at high risk of stroke.
- Chelation agents (1st IV or sub q then PO) to decrease the impact of iron overload on patients receiving monthly transfusions or apheresis for the same indication.
- Hydroxyurea for prevention of painful episodes and other complications.

The only available cure is hematopoietic stem cell transplant.

Presentation

- SCD is included in newborn screens for early detection, referral and diagnosis.
- Symptoms, like pain, associated with SCD do not usually present during first 6 months because of the presence of Fetal Hemoglobin (HgbF). Thus, a common treatment for SCD, hydroxyurea, is aimed at increasing the amount of HgbF circulating and decreasing sickle HgB.
- Since this lifelong disease begins in infancy, parents or caregivers are key to providing care, understanding and assessing for disease complications and seeking early treatment for the child.

Sickle Cell Disease Management

SCD: Management

1. **Supportive management**: maintain the essential requirements for good health, such as balanced diet, sleep, hydration, folic acid, regular follow-ups, etc.
2. **Symptomatic management**: targeted to alleviate the symptoms of the disease as they occur. These include blood transfusion for symptomatic anemia, analgesics for pain, antibiotics for infections, etc.
3. **Preventative management**: to prevent complications of the disease. These include vaccination, avoidance of stressful situations, Hb F induction with hydroxyurea or other agents, transfusion to prevent the recurrence of stroke, etc.
4. **Abortive management**: to abort painful crises, thus preventing them from getting worse or precipitating other complications.
5. **Curative therapy**: stem cell transplantation. Gene therapy remains a challenging possibility.

SCD: Nociceptive pain

Sickled RBCs can obstruct flow in small blood vessels, blocking and impairing oxygen delivery to tissues and organs, causing episodes of pain referred to as vaso-occlusive crisis (VOC).

In combination, deformable RBCs, increased viscosity, endothelial activation and vasoconstriction cause ongoing vaso-occlusion in the microvasculature. Vaso-occlusion leads to hypoxia, ischemia, and eventually tissue damage followed by chronic vascular inflammation.

SCD is characterized by chronic intravascular and extravascular hemolysis, which leads to liberation of free hemoglobin, which then disrupts the arginine-nitric oxide pathway, leading to sequestration of nitric oxide released from the vascular endothelium.

The combination of hypoxia and reperfusion injury, ischemic tissue damage and inflammation is unique to pain of sickle cell disease.

SCD: Nociceptive Pain

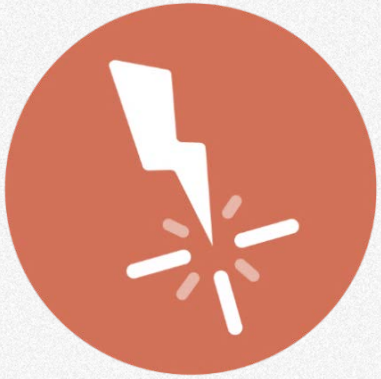
Vaso-Occlusive Events

Pain from SCD is thought to be primarily due to somatic and visceral tissue injury from vaso-occlusive events.

- Somatic and visceral cellular tissue injury releases pro-inflammatory cytokines, potassium ions and histamine; bradykinin is degraded from plasma kininogen, a component of inflammatory exudate.
- Platelet activation release serotonin.
- Phospholipids liberated from damaged cells initiate the arachidonic acid cascade.
- 5-lipooxygenase and cyclooxygenase synthesize leukotrines and prostaglandins.
  - These chemical byproducts of cellular damage activate nociceptors on the peripheral afferent (transduction) initiating an action potential and transmitting it along A delta and C fibers to the dorsal horn of the spinal cord.
- The primary afferent nociceptors also release calcitonin gene related peptide (CGRP), norepinephrine and substance P.
- Substance P sensitizes peripheral afferents, dilating nearby blood vessels, leading to local edema and the release of histamine from mast cells.
- Leukotrines and prostaglandins also sensitize nociceptive peripheral afferents to be activated by typically non-painful stimulus (allodynia) during an inflammatory response.

Subsequent ischemia and activation of inflammatory pathways lead to pain of varying intensity.

SCD: Neuropathic Pain



Neuropathic pain results from damage or abnormal communication within the peripheral or central nervous system and is characterized by:

- Allodynia-pain elicited from non-painful stimuli, such as light touch
- Hyperalgesia-enhanced pain from painful stimuli.

Evidence from transgenic mice and reports of pain quality from adults with SCD challenge the theory that SCD pain is from visceral and somatic tissue injury following vaso-occlusion, suggesting a component of SCD pain is neuropathic.

CNS neuroplasticity occurs after neuronal damage, resulting in central sensitization.

Excessive nociceptive signals bombarding the CNS from the periphery cause changes both in the spinal cord and in the brain. The result is continuous amplification of pain sensation. Clinical manifestations of central sensitization include:

1. reduced pain threshold resulting in hyperalgesia and allodynia,
2. expanded receptive fields refers the hyperalgesia beyond the area of original injury;
3. pain sensation continues after the original injury.

SCD: Pain Prevalence

A hallmark symptom of SCD is pain

Pain is often the first sign of the disease and other illnesses: Infection, acidosis, hypoxia, dehydration, extreme temperature changes.

Pain associated with SCD is

- Unpredictable
- Sudden Onset
- Recurrent
- Any and all locations: joint, abdomen, limb, back, headache
- Worse than postoperative pain and is as intense as terminal cancer pain.

The burden of pain worsens as children transition from childhood to adolescence and young adulthood, making the treatment of SCD-related pain in childhood critically important for interrupting potential negative cycles of pain and disability.

Individuals with SCD suffer from recurrent episodes of severe, unrelenting pain – acute vaso-occlusive pain crises (VOC). Screening programs, vaccination, antibiotic prophylaxis and education have reduced the childhood mortality from SCD, but there has been little progress in reducing the burden of pain for individuals with SCD.

Children with SCD experience:

- VOC
- Everyday pain as other children such as bumps and bruises
- Post-operative pain with increased frequency of surgical procedures: e.g. splenectomy following splenic sequestration; cholecystectomy
- Abdominal pain from splenic sequestration- can occur in infants, toddlers and preschool children
- Chest pain from Acute Chest Syndrome (chest pain, infiltrates, hypoxia) with respiratory infections, asthma exacerbation or after surgery.

SCD: Pain Prevalence

The Pain in Sickle Cell Epidemiology Study (PISCES)

PISCES documented pain as a common experience for adults with SCD.

- 55% reported pain on more than half the days studied
- 29% reported pain on over 95% of the days.
- Prescribed opioids are used by >80% of adults with SCD on 78% of home pain days

Even though >50% of adults with SCD report severe pain almost every day, they also report NOT seeking medical care for severe pain >90% of the time. ***Failure of adults to seek medical care for severe pain is a learned response.***

In hospital, severe acute pain from SCD is treated with escalating doses of the same opioids that are available to patients with SCD at home. Repeated experiences of the ineffectiveness of this treatment strategy may lead patients with SCD to conclude that seeking treatment for severe pain is futile.

AND

Repeated use of opioids leads to central sensitization and hyperalgesia.

Reports of severe pain and opioids use at home are far less in children and adolescents with SCD.

Children and adolescents with SCD report pain at home on about 9% of 1515 days surveyed.

New strategies are needed to break the cycle of SCD pain and prevent long-term consequences of repeated acute pain crises, ineffective treatment, and opioid use, specifically central sensitization, hyperalgesia and chronic pain.

Christopher

What next steps would you recommend?

Christopher reports the following pain control steps taken at home:

- *He took ibuprofen every day this week, but today he took at least a dozen morphine pills that did not work.*
- *You review the prescription drug monitoring program and ask him where he got the morphine and why he didn't take the hydrocodone he was given 3 weeks ago.*
- *He went to school every day, but was too tired to do homework and just tried to lay down on a heating pad and rest.*
- *He says he needs 5mg of IV dilaudid and Benadryl.*

SCD: Pain Phases

Children with acute VOC are typically hospitalized for 4 days/crises.

- Pain severity and older age have been identified as risk factors for readmission within 30 days of hospitalization for pediatric patients with SCD.
- Older pediatric age is also a risk factor for longer lengths of stay.
- More frequent and severe SCD pain is related to diminished physical function, poor health-related quality of life, and higher health service use in children.

Clinical descriptions of VOC requiring hospitalization are documented as evolving through 4 phases:

1. **Prodromal** phase lasts 1-2 days. Individuals with SCD describe symptoms of numbness, paresthesia or aches at the location of subsequent pain.
2. **Initial** phase lasts approximately 2 days. Individuals with SCD report increasing pain. Often inflammatory markers (erythrocyte sedimentation rate (ESR) and (CRP) C-reactive protein) are also increased.
3. **Established** phase lasts approximately 4 days and is associated with maximum pain severity, increasing ESR and peak CRP.
4. **Resolving** phase is described by lessening pain, peak in ESR, and decreasing CRP.

Despite escalating doses of opioid analgesics, pain intensity scores do not significantly decrease during hospitalization (Zempsky, et al, 2008).

SCD: Pain Management

Principles of pain management

- Use developmentally appropriate pain assessment strategies
- Conduct a thorough pain assessment
- Determine the patient's and family's goals of care
- Incorporate multimodal therapies
- Prevent or rapidly treat adverse effects
- Reassess frequently and change therapies if needed
- Educate patients, families, other caregivers

Goals of pain management associated with SCD

Pain management is focused on efforts to prevent, eliminate, and/or reduce painful sensations. It includes both pharmacological and biobehavioral methods to effectively control or alleviate pain so patients can live life with optimal quality.

- Prevention
- Decrease pain
- Prevent/manage adverse effects associated with treatment
- Promote patient safety and function
- Enhance quality of life

Treatment of Sickle Cell Disease Pain

Pharmacologic Treatment

NIH-NHLBI expert panel report on sickle cell disease management (2014)–ED VOC pain management recommends:

- IV analgesic within 30 minutes of triage or within 60 minutes of registration.
- Pain reassessment and medication titration every 15-30 minutes until pain is under control.
- Obtaining IV access may delay prompt treatment of severe acute pain; intranasal administration of opioids with a particulate diffuser may be an acceptable alternative for the child with VOC.

Acute VOC is routinely treated with:

- Non-steroidal anti-inflammatory drugs (NSAIDs)
- High doses of opioids including IV opioid delivered by patient controlled analgesia (PCA) and continuous infusions of IV opioids.
- Anticipate opioid doses will be higher than recommended starting doses in patients with SCD who have been routinely treated with opioids.
- Start PCA according to individualized management plan and adjust according to response.
- Maintain home medications throughout hospitalization.

Pharmacologic Treatment

Drugs that block the production or release of the by-products of cellular damage may inhibit the transmission of pain.

- Corticosteroids and ketoprofen inhibit leukotrienes synthesis
- NSAIDS and aspirin inhibit prostaglandin synthesis
- Antihistamines inhibit histamine release.

Opioids

- Enhance the inhibition of endorphins at the peripheral afferent nociceptive terminals,
- Bind to the mu & delta receptors at the spinal cord, and
- Inhibit substance P and glutamate at the spinal cord and brain.

Antidepressants inhibit the reuptake of serotonin & norepinephrine, and thereby the sensitization of the nociceptors.

Alpha 2 adrenergic agonists inhibit wind up.

Benzodiazepines also inhibit the facilitation of wind up by GABA a.

Ketamine inhibits substance P and glutamate at the spinal cord.

Pharmacologic Treatment

Morphine is not a panacea

Is morphine the gold standard for the treatment of severe VOC?

Patients with SCD often require hospitalization for a continuous infusion of morphine that may cause significant pruritus. Simultaneous continuous infusion of naloxone with morphine in pediatric patients with SCD is feasible and well tolerated.

- Seizures from morphine have a reported prevalence of 1.2% and may occur when given in sufficiently large doses.
- Morphine is the most histaminergic opioid, associated with severe pruritus in some patients.
- Morphine use in patients with SCD seems to be associated with acute chest syndrome.
- Side effects include nausea, vomiting, pruritus, constipation, mental changes, tolerance, dependence, hyperalgesia, and opioid use disorder.
- Morphine and it's metabolite, morphine-6-glucuronide, are both renally excreted, requiring monitoring of renal function and cautious use in those with renal impairment.

Therefore, choice of opioid, route and dose should be individualized and patients monitored for possible side effects and misuse, or diversion.

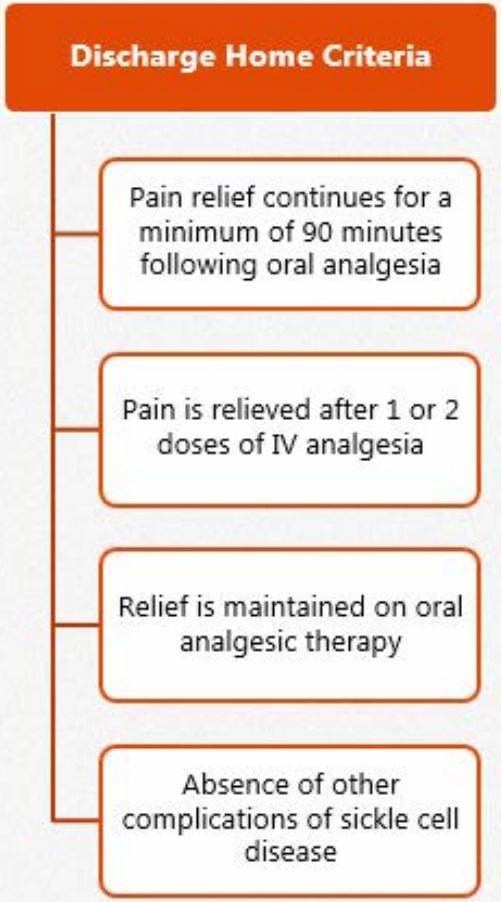
Christopher

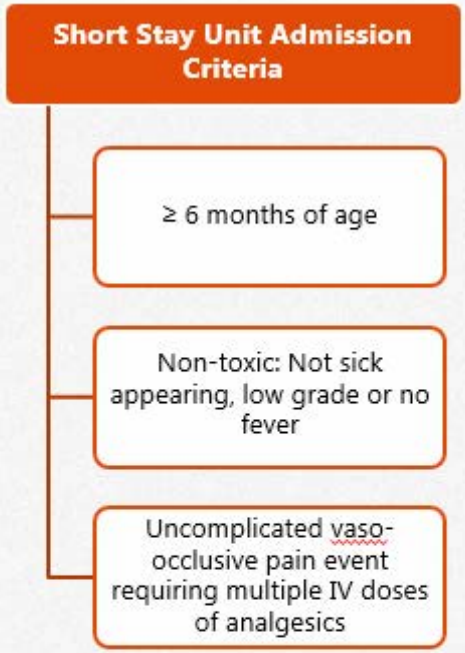
What would you expect to do to manage his pain?

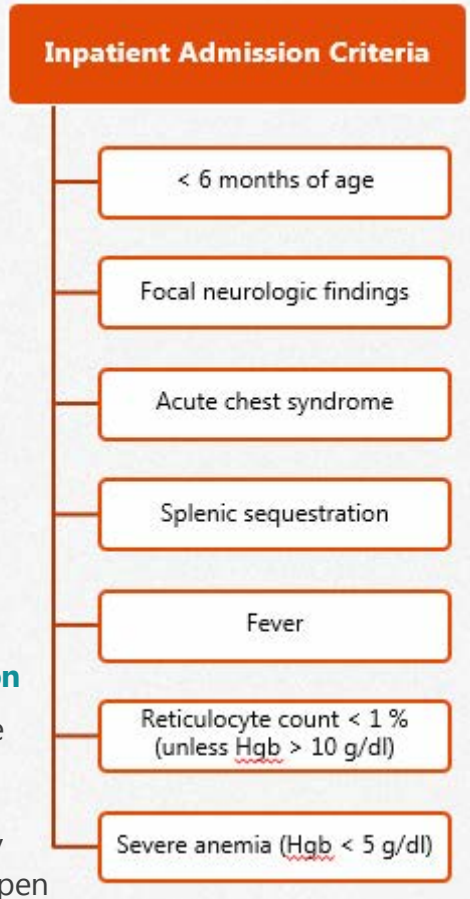
A secondary analysis of data collected on 204 youth (mean age 13.6 yrs.) with SCD pain presenting to the ED and admitted to the hospital from 8 different sites was preformed.

Earlier start of oral opioids was highly associated with shorter hospital stay and higher HRQOL.

Admit or Discharge







Guidelines for treatment & admission

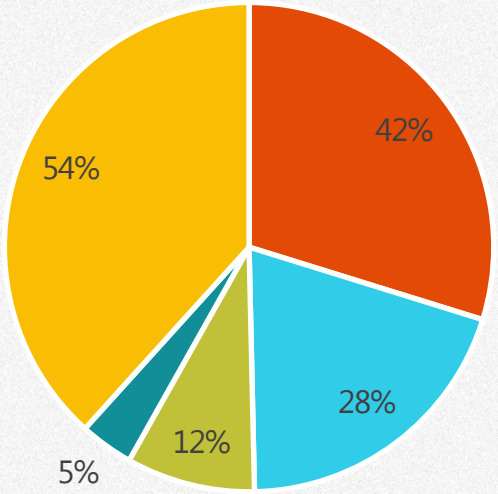
Note that different hospitals may have different practices. In some settings, especially those with comprehensive SCD centers, there may be a short stay unit or day hospital. These are often open until 5 or 6 pm. Patients with SCD may be treated in these settings without hospital admission or overnight stays. These settings are better prepared to care for patients with VOC pain than EDs because they are often staffed with clinicians who are familiar with patients with SCD and their care plan.

Infants and young children with SCD-SS who present to the ED with fever are usually admitted. Sepsis with fever and dehydration is a significant concern due to their inadequate immune systems. Some hospitals have fever reduction protocols to monitor patient status and avoid hospital admission of all infants and young children with SCD and fever.

Biobehavioral Treatments

Pediatric Patients with SCD
Use of Biobehavioral Strategies

- Prayer
- Lifestyle/Mind-Body Therapies
- Biochemical
- Massage
- Complementary and Alternative Therapies



Physical techniques

- Heat
- Massage
- Repositioning/bracing

COLD is contraindicated and may precipitate VOC.

Cognitive/behavioral therapies

- Relaxation/guided imagery
- Distraction
  - Distraction includes talking to friends. Therefore, socializing should be considered a positive coping strategy rather than evidence to negate the patient with SCD self-report's of severe pain.
- Expressive arts/music
  - Allows expression of pain and emotions in a way that is nonverbal.
- Cognitive reframing

Cognitive/behavioral therapies

- Support groups
  - Support groups assist patients to understand the universality of their experiences and learn coping strategies from others in similar situations.
- Spiritual counseling/prayer

Study by Sibinga et al, 2006. 57 parents of children with SCD participated in a phone survey of the use of biobehavioral strategies with their child with SCD

Coping Strategies

Some strategies put the child who is hurting in control while others are more passive techniques.

Learning and using active coping strategies gives the child power to help him or herself when in pain.

Active coping involves doing something to help, like :

- taking a warm bath
- thinking about something (distraction)
- playing a video game
- listening to music
- gaining control - getting help with the pain or using positive self-talk statements.

Christopher

What biobehavioral therapies might be useful for Christopher?

Which biobehavioral therapies are contraindicated?

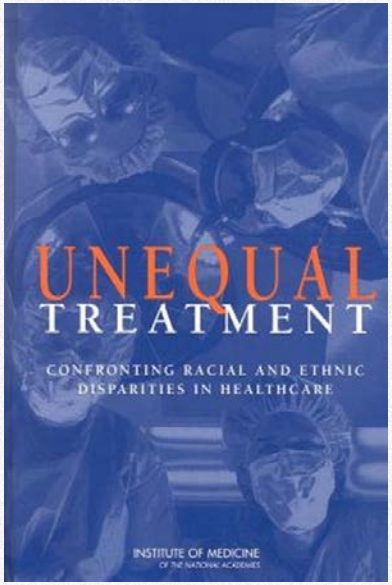
What education would be helpful to provide to Christopher and his family?

Type your answer here.

Health Care Disparities

Beware of Health Care Disparities

- Sickle cell disease is not solely a disease of individuals of African descent. However, in the United States it is most prevalent among African Americans.
- African Americans in general are also disproportionately more likely to receive differential health care and experience worse health outcomes.
- This was illustrated convincingly in the 2003 Institute of Medicine Report: "Unequal Treatment" that demonstrated that African Americans receive poor care in virtually all healthcare and treatment settings in the U.S.

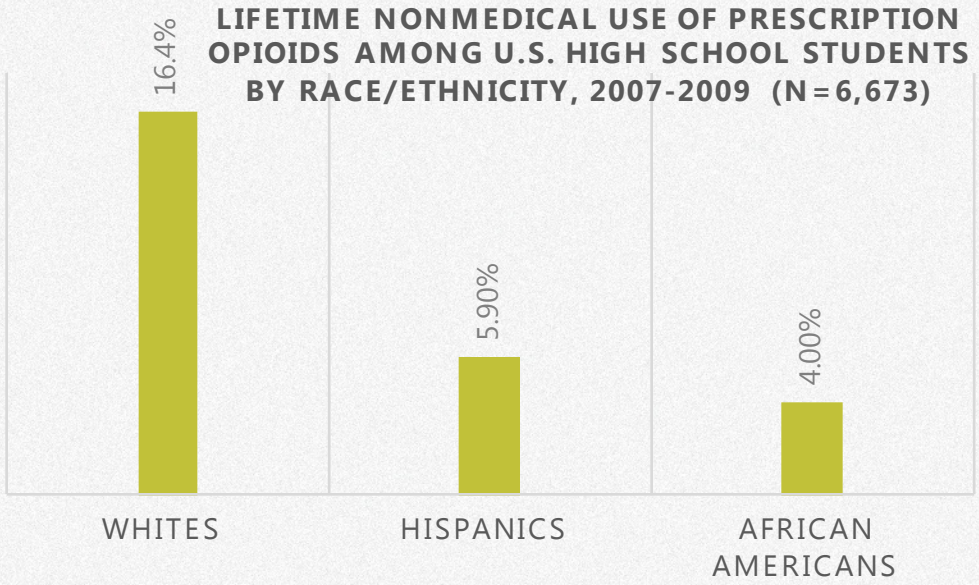


Institute of Medicine. Unequal treatment: Confronting Racial and Ethnic Disparities in Healthcare. Washington DC: National Academy Press; 2003.

Nonmedical Use of Prescription Opioids

Contrary to common belief, non-medical use of "prescription opioids" is not highest among African Americans.

The estimated lifetime prevalence of any medical use of prescription opioids was 22.8% among White students, 6.9% among African-Americans and 6.7% among Hispanics ($P < 0.001$) while the lifetime prevalence of Non Medical use of prescription opioid (NMUPO) was 16.4% among White students, 4.0% among African-Americans and 5.9% among Hispanics ($P < 0.001$).



As shown here, there were notable racial/ethnic differences with respect to the history of medical use and NMUPO: white students had significantly higher rates of both medical use and NMUPO compared to African-Americans and Hispanics, and correspondingly significantly lower rates of non-use.

This data provides relevant information to challenge perceptions about opioid abuse and misuse.

Raw data: McCabe SE, et al. Arch Pediatr Adolesc Med. 2012;166(9): 797–802.

Provider Bias

Recognize most patients try to manage their care at home and come to the hospital only as a last resort when in need of IV medication for treatment.

Clinician judgement about VOC can introduce a bias that affects pain treatment for children with SCD.

Bias about believing pain self report.

Contributing factors:

- high pain intensity scores with minimal outward signs of pain,
- racial or ethnic bias,
- concern about drug addiction or drug seeking.

Bias creates a lack of trust and poor communication between the person with SCD and the treating clinicians(s).

Patient Bias

Because SCD pain is a lifelong condition and episodes increase over time, consequences of inadequate care and distrust can build up.

Solutions include:

- consistent relationship,
- use of established pain management protocols that incorporate evidence based guidelines consistently,
- individualized protocols for pain management

Keep a home diary or record of how pain is managed at home prior to coming to the ED.

Photographic Numeric Oucher Pain Tool

Acute and procedural pain

Since children with SCD are primarily African American or Hispanic, this tool provides children of these ethnicities the ability to relate to faces similar to their own.

100 African-American children with SCD rated preference of 3 scales:

- Wong Baker FACES -- 56%
- Black Oucher -- 26%
- VAS -- 18%

Validity was strongest for FACES, then Oucher and VAS.

Self Portrait

Self Portrait by an adolescent with SCD-SS depicting "usual" self and self when experiencing VOC pain.

This artist has drawn how she feels inside when having a VOC pain episode. Obviously, she actually does not show these outward signs of pain. The "story" here is the silent suffering that can accompany acute sickle cell pain.

Effects of VOC Episodes on Health-Related Quality of Life (HRQOL)

"To have great pain is to have certainty; to hear that another person has pain is to have doubt."

-Scarry, The Body in Pain, 1985, p.7.

VOC negatively impacts HRQOL in all domains

Negative effects of pain episodes in patients with SCD are reported by both children and parents:

- decreased functioning
- increased fatigue
- decreased school performance.

Emotional distress is also an important contributor to both physical and mental HRQOL.

Sociodemographic variables and barriers to care must also be considered.

How do your personal experiences, beliefs, and/or attitudes influence your pain assessment and care for patients with SCD?

Type your answer here.

Christopher

What barriers may prevent Christopher from adhering to this discharge plan?

How can you break down these barriers?

Discharge from ED

A follow-up appointment is arranged with Hematology in 3-5 days unless symptoms worsen.

Christopher is sent home with prescriptions for an opioid and ibuprofen as needed.

Follow-up

Christopher

Christopher's current medications:

- *Folic acid 1 mg daily*
- *Vitamin D 1,000 IU daily*
- *Hydroxyurea: 20 mg/kg/day*
- *PRN Ibuprofen and oral opioid*

What coping skills will help Christopher with HRQOL?

During his hematology office visit for hospital follow-up, Christopher reports his current pain is "manageable." His pain includes aching of his legs and lower back, but he has been attending school, and he does not take pain medicines everyday.

Physical exam:

- *New finding of hip pain Avascular necrosis (AVN) of femoral head is suspected and needs to be evaluated and treated. Physical therapist can assist with evaluation to help with ROM, adaptive exercise.*
- *Orthopedic evaluation will help confirm the diagnosis. Treatment starts conservatively with PT followed by surgical intervention .*

Hydroxyurea for Prevention of VOC and Other SCD Complications

The utility of hydroxyurea for all patients with Sickle Cell Anemia (SCA) is clear and indisputable. With documented efficacy and acceptable long-term safety profile, hydroxyurea treatment is considered the gold standard of care for all young patients with SCA.

Hydroxyurea is an antineoplastic agent and a potent inducer of fetal hemoglobin.

- Adult SCD patient clinical trials demonstrated effectiveness for increasing fetal hemoglobin production and decreasing total WBC without significant bone marrow suppression.
- BABY HUG study - Phase 3 clinical trial testing Hydroxyurea versus placebo in young children with SCD (ages 9-18 months at start of trial).

RECENT FINDINGS: The phase III study of hydroxyurea in infants (BABY HUG) has just been completed and preliminary results indicate equivocal benefits for organ protection during the 2-year treatment period, but significant benefits for pain, acute chest syndrome, hospitalizations, and transfusions. Three new reports document the benefits of hydroxyurea on reducing mortality in SCA: two adult trials (LaSHS and MSH) and one pediatric study (Brazilian cohort). Recent results from the HUSTLE protocol suggest minimal genotoxicity or carcinogenicity with long-term hydroxyurea exposure.

SUMMARY: Exporting our knowledge and experience with hydroxyurea to developing nations with large medical burdens from SCA can help relieve global suffering.

.This clinical trial is registered with the National Institutes of Health (NCT00006400, www.clinicaltrials.gov)

Christopher

What education should be provided to Christopher and his family?

Hematology office visit for hospital follow-up

Physical findings:

- *Paraspinal muscle spasms*
- *Flank tenderness on palpation*
- *Limping on ambulation – left hip pain*
- *Orthopedic and PT referral for evaluation*

New Diagnosis:
Avascular necrosis (AVN) of femoral head

Resources: Web Sites for Education for Families and Others

There are a variety of websites that might provide assistance with coping

Starlight Children's Foundation

https://www.starlight.org/

Sickle Cell Kids

http://Sicklecellkids.org

University of Michigan Medicine: Pain in Sickle Cell Disease

http://www.med.umich.edu/yourchild/topics/sicklecell.htm

Apps

A smart phone app to use as a pain diary for personal tracking of symptoms and care may also be useful.

In Summary…

Key Points

Acute pain is the hallmark and most frequent reason for hospitalization of children with SCD.

SCD Management

1. **Supportive management**
2. **Symptomatic management**
3. **Preventative management**
4. **Abortive management**
5. **Curative therapy**

Sickle Cell Disease (SCD)

- SCD is an inherited, autosomal, recessive disorder where hemoglobin has an amino acid change (Glutamate →Valine) in the β globin chain resulting in polymerization, causing the red blood cells to assume a sickled shape.
- SCD is the most common inherited disorder, with millions of people worldwide who suffer from this disease.
- The only available cure is hematopoietic stem cell transplant.
- Since this lifelong disease begins in infancy, parents or caregivers are key to providing care, understanding and assessing for disease complications and seeking early treatment for the child.

Pain prevalence

- Pain from SCD is thought to be primarily due to somatic and visceral tissue injury from vaso-occlusive (VOC) events.
- Pain associated with SCD is unpredictable, sudden onset, recurrent, at any and all locations (joint, abdomen, limb, back, headache), and worse than postoperative pain and is as intense as terminal cancer pain.

Goals of pain management associated with SCD

Pain management is focused on efforts to prevent, eliminate, and/or reduce painful sensations; Includes both pharmacological and biobehavioral methods to effectively control or alleviate pain so patients can live life with optimal quality.

Appendix

References

Ataga, K. I., Kutlar, A., Kanter, J., Liles, D., Cancado, R., Friedrisch, J., Guthrie, T.H., Knight-Madden, J., Alvarez, O.A., Gordeuk, V.R., Gualandro, S., Colella, M. P.,Smith, W.R. , Rollins, S.A., Stocker, J.W. and Rother R.P. (2017). Crizanlizumab for the prevention of pain crises in sickle cell disease. The New England Journal of Medicine, 376(5), 429-439.

Ballas, S. K., Kesen, M. R., Goldberg, M. F., Lutty, G. A., Dampier, C., Osunkwo, I., .Wang, W. C., Hoppe, C., Hagar, W., Darbari, D. S. and Malik, P. (2012). Beyond the definitions of the phenotypic complications of Sickle Cell Disease: An update on management. The Scientific World Journal Volume 2012, Article ID 949535, 55 pages doi:10.1100/2012/949535.

Brandow, A. M., Nimmer, M., Simmons,T., Casper T. C., Cook, L. J.,Chumpitazi,C. E., Scott, J. P., Panepinto, J. A. and Brousseau, D. C. (2016). Impact of emergency department care on outcomes of acute pain events in children with sickle cell disease, American Journal of Hematology , 91 (12), 1175-1180. DOI: 10.1002/ajh.24534.

Brandow, AM, Brousseau, D. C., Pajewski, N. M. and Panepinto, J. A. (2010). Vaso-Occlusive painful events in Sickle Cell Disease: Impact on child well-being. Pediatric Blood and Cancer; 54(1), 92-97.

Buchanan ID, Woodward M, Reed GW. Opioid selection during sickle cell pain crisis and its impact on the development of acute chest syndrome. Pediatr Blood Cancer. 2005;45(5):716-724.

Dampier, C., Ely, B., Aertker, K., Kesler, K., Brodecki, D., & Coleman, C. (2011). Longitudinal analysis of vaso-occlusive pain in young children with sickle cell disease. The Journal of Pain, 12(4), supp 2, p25. Update to paper.

Dampier, C., Ely, B., Brodecki, D.& O'Neal P. (2002). Characteristics of pain managed at home in children and adolescents with sickle cell disease. Journal of Pain, 3(6), 461-470.

Dampier, C., Ely, B., Brodecki, D., Coleman, C., Aertker L., Sendecki, J. A., Leiby, B., Kesler, K., Hyslop, T., & Stuart, M.(2013). Pain Characteristics and Age-Related Pain Trajectories in Infants and Young Children with Sickle Cell Disease, Pediatric Blood and Cancer, DOI 10.1002/pbc.24796.

Dampier, C., Ely, E., Eggleston, B., Brodecki, D. & O'Neal, P (2004). Physical and cognitive-behavioral activities used in the home management of sickle pain: A daily diary study in children and adolescents. Pediatric Blood and Cancer, 43(6), 674-678.

Dampier, C., Lieff, S., LeBeau, P., Rhee, S. McMurray, M., Rogers, Z., Smith-Whitley, K., and Wang, W., the Comprehensive Sickle Cell Centers (CSCC) Clinical Trial Consortium (CTC) Site Investigators (2010). Health-Related quality of life in children with sickle cell disease: A report from the Comprehensive Sickle Cell Centers Clinical Trial Consortium. Pediatric Blood and Cancer; 55(3): 485–494. doi:10.1002/pbc.22497.

Ely, B., Dampier, C., Gilday, M., O'Neal, P. & Brodecki, D. (2002). Caregiver report of pain in infants and toddlers with sickle cell disease: Reliability and validity of a daily diary. Journal of Pain, 3(1), 50-57.

Emotional Distress, Barriers to Care, and Health-Related Quality of Life in Sickle Cell Disease. Marsha J. Treadwell, PhD, Fernando Barreda, BA, Kimpreet Kaur, BS, and Ginny Gildengorin, PhD.

Institute of Medicine. Unequal treatment: Confronting Racial and Ethnic Disparities in Healthcare. Washington DC: National Academy Press;2003.

Jacob, E., Stinson, J., Duran,J. Gupta,A, Gerla, M., Lewis, M., & Zeltzer, L. (2012). Usability Testing of a Smartphone for Accessing a Web-based e-Diary for Self-monitoring of Pain and Symptoms in Sickle Cell Disease, Journal of Pediatric Hematology, 34:326–335.

Koch J, Manworren R, Clark L, Quinn CT, Buchanan GR, Rogers ZR, Pilot study of continuous co-infusion of morphine and naloxone in children with sickle cell pain crisis. Am J Hematol. 2008 September ; 83(9): 728–731. doi:10.1002/ajh.21213.

Kopecky EA, Jacobson S, Joshi P, Koren G. Systemic exposure to morphine and the risk of acute chest syndrome in sickle cell disease. Clin Phar-macol Ther. 2004;75(3):140-146.

Lee, M. T., Licursi, M., and McMahon, D. J. (2015). Vitamin D deficiency and acute vaso-occlusive complications in children with sickle cell disease. Pediatric Blood and Cancer, 62, 643–647.

Lewing K, Britton K, DeBaun M, Woods G. The impact of parenteral narcotic choice in the devel-opment of acute chest syndrome in sickle cell dis-ease. J Pediatr Hematol Oncol. 2011;33(4):255-260.

Luffy R, Grove SK. Examining the validity, reliability, and preference of three pediatric pain measurement tools in African-American children. Pediatr Nurs. 2003;29:54-9. PubMed PMID: 12630508.

McGann, P.T. and Ware, R. E. Hydroxyurea for sickle cell anemia: what have we learned and what questions still remain? Current opinion in Hematology, 18: 158-165.

NHLBI Expert Panel Report on the Management of Sickle Cell Disease. http://www.nhlbi. nih.gov/sites/www.nhlbi.nih.gov/files/sickle-celldisease-report.pdf; 2014.

Scarry, E. The Body in Pain: The Making and Unmaking of the World. Oxford University Press; 1987.

Sibinga, E., Shindell, D., Caselle, J. F., Duggan, A. K., and Wilson, M. H. (2006). Pediatric patients with sickle cell disease: Use of complementary and alternative therapies. The Journal of Alternative and Complementary Medicine, 12(2), 291–298.

Sickle cell disease. Genetics Home Reference. 2013. Available at: http://ghr.nlm.nih.gov/condition/sickle-cell-disease Accessed on March 18, 2017.

Sobota, A., et al. (2012). Thirty-day readmission rates following hospitalization for pediatric sickle cell crisis at freestanding children's hospitals: risk factors and hospital variation. Pediatric Blood and Cancer; 58(1): 61-65.

Summary of evidence pediatric behavioral or self report pain assessment tools: www.IMMPACT.org.

U.S. National Library of Medicine. Sickle cell disease. Genetics Home Reference. 2013. Available at: http://ghr.nlm.nih.gov/condition/sickle-cell-disease Accessed on March 19, 2017.

Wallen et al. Sleep disturbance, depression and pain in adults with sickle cell disease. BMC Psychiatry 2014, 14:207 http://www.biomedcentral.com/1471-244X/14/207.

What is Sickle Cell Disease? And National Sickle Cell Awareness Month with NHLBI.

https://www.nhlbi.nih.gov/about/directorscorner/messages/national-sickle-cell-awareness-month-nhlbi Accessed March 18, 2017.

Zempsky, W. (2009). Treatment of sickle cell pain: Fostering trust and justice. Journal of the American Medical Association. 302(22), 2479-2480