Improving Patient Outcomes and Healthcare Systems of Care for Individuals with Sickle Cell Disease

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OBJECTIVES

1. Provide an overview of research to improve outcomes for individuals with sickle cell disease in the emergency department (ED) setting.

2. Review a RCT to improve treatment of vaso-occlusive episodes

3. Review research to identify unmet social behavioral health needs in the ED will be discussed.
What Is Sickle Cell Disease?

• An inherited disease of red blood cells
• Affects hemoglobin
• Polymerization of hemoglobin leads to a cascade of effects decreasing blood flow
• Tissue hypoxia causes acute and chronic damage
• Abnormalities in platelets and WBCs as well
Epidemiology of SCD

• The most common rare (orphan) disease
• SCD is a genetic disease affecting 70,000 – 100,000 Americans, primarily of African descent (Hassell, 2010)
• Most common genetic disease among blacks
• SCD occurs in 1 of every 500 black births

Global Presence & Mortality of SCD

• High global burden anticipated to increase
• In 2010, estimated global number of individuals with SCD 5,476,000
• Estimated 300,000 births/year
• SCD is most prevalent in Africa, South Asia and the Middle East where malaria is endemic
• In some African countries between 10-40% of individuals carry the gene, estimated prevalence of 2%
• Countries with the highest burden are predicted to include: Nigeria, Democratic Republic of Congo, and India
• Interventions including newborn screening, penicillin prophylaxis and immunizations can improve morbidity and mortality worldwide


Distribution of hemoglobin disorders like sickle cell anemia around the world
By births of affected babies per 1,000 births
Epidemiology of SCD

Pain Management

Rule out other sources of pain than VOE while treating VOE

- Acute chest syndrome
- Splenic sequestration
- Abdominal catastrophes

Treat pain aggressively

- Try to contact patients’ SCD physician for analgesic suggestions, however, DO NOT delay administration of analgesics.
- Administer first dose as soon as possible given triage and healthcare resources, ideally within 30 min of triage or 60 min of registration.
- Administer intravenous opioids (morphine sulfate or hydromorphone)
- Use individualized doses, and when not possible, use a standard SCD protocol

Pain Management

Treat pain aggressively (cont.)

• Use the **subcutaneous route** if obtaining IV access will significantly delay administration of first dose, & when IV access is not possible. Avoid intra-muscular route due to tissue damage and erratic absorption.

• Use individual/personalized analgesic dosing plans if & when available (Electronic medical records).

• Use weight based dosing when plan is not available (see tables)

• Allow patient to continue long-acting opioids if prescribed as an outpatient.

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• Explore the change in pain scores from arrival to discharge between patients with VOE randomized to a standard SCD (control) or patient-specific analgesic protocol; and

• Determine differences in secondary (pain experience, hospital utilization, side effect and safety) outcomes.
Methods

• Design: Randomized controlled trial
• Setting: 2 busy urban ED’s
• Sample: Adults with vaso-occlusive episodes (VOE), up to 5 emergency department (ED) visits
• Methods:
  ▪ Patients were pre-enrolled
  ▪ Randomized to receive either an individualized dosing or weight based dose in accordance with the National Heart, Lung and Blood Institute (NHLBI) recommendations for VOE
  ▪ Protocol was loaded into electronic health record
  ▪ At next ED visit, protocol was followed
  ▪ Patients were interviewed by research staff, q 30 minutes from placement until discharge, or 6 hours
Outcomes

Primary Outcome

• Change in pain score (0-100 mm VAS) from arrival to discharge, defined as decision to admit to hospital, discharged home, or 6 hours from placement in ED room.

Secondary Outcomes

• Safety: vital signs, sedation scores, side-effects
• Pain satisfaction with pain management questions
Consort

Enrollment

Assessed for eligibility (N=168 patients)

Excluded (n=116)
  • Not meeting inclusion criteria (n=67)
  • Declined to participate (n=49)
  • Other reason(s) (n=0)

Randomized (N=106 enrolled patients)

Allocation
Consort Diagram

**Allocation**
- Patient-specific
  Allocated to intervention (N=53 patients)
- Standard Weight-based
  Allocated to intervention (N=53 patients)

**ED Study Visits**
- Patient-specific
  26 patients contributed ED visit data and received allocated intervention for a total of 62 ED visits
  - 26 patients had no ED visits
  - 1 patient withdrew after randomization
- Standard Weight-based
  26 patients contributed ED visit data and received allocated intervention for a total of 62 ED visits
  - 26 patients had no ED visits

**Analysis**
- Patient-specific
  Analyzed (N=26 patients) (62 ED visits)
- Standard Weight-based
  Analyzed (N=26 patients) (64 ED visits)
## Results

<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td><strong>PRIMARY OUTCOME</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Change in pain scores from arrival to discharge (adjusted means)</td>
<td>42.7 ± 7.2</td>
<td>27.1 ± 0.5</td>
<td>15.6 ± 5.0</td>
<td>0.002</td>
</tr>
<tr>
<td>Change in pain scores from arrival to discharge (unadjusted means)</td>
<td>42.4 + 30.7</td>
<td>27.1 + 23.4</td>
<td>15.4 + 27.3</td>
<td>0.003</td>
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<td>------------------------------------------------------------------------</td>
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<tr>
<td><strong>SECONDARY OUTCOMES</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pain Related</td>
<td></td>
<td></td>
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</tr>
<tr>
<td>ED visit with a $\geq 13$ mm reduction (clinically relevant) in pain scores from arrival to discharge (unadjusted scores)</td>
<td>82%</td>
<td>71%</td>
<td>11%</td>
<td>0.15</td>
</tr>
<tr>
<td>Patient’s self-identified goal for pain score met</td>
<td>35%</td>
<td>25%</td>
<td>10%</td>
<td>0.2</td>
</tr>
<tr>
<td>Patient reports need for more pain medicine</td>
<td>55%</td>
<td>67%</td>
<td>12%</td>
<td>0.123</td>
</tr>
<tr>
<td>Patient’s satisfaction with ED pain management</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Very dissatisfied</td>
<td>7%</td>
<td>9%</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Somewhat dissatisfied</td>
<td>16%</td>
<td>25%</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Somewhat satisfied</td>
<td>46%</td>
<td>53%</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Very satisfied</td>
<td>31%</td>
<td>14%</td>
<td>---</td>
<td>---</td>
</tr>
<tr>
<td>Hospital admission for VOE pain control</td>
<td>40%</td>
<td>58%</td>
<td>18%</td>
<td>0.037</td>
</tr>
<tr>
<td>Hospital readmission for VOE in 72 hours</td>
<td>13%</td>
<td>10%</td>
<td>3%</td>
<td>0.527</td>
</tr>
<tr>
<td>ED re-visit for VOE in 72 hours</td>
<td>15%</td>
<td>6%</td>
<td>9%</td>
<td>0.1545</td>
</tr>
</tbody>
</table>
COMPARE VOE
A Comparison of Individualized vs. Weight Based Protocols to Treat Vaso-occlusive Episodes in Sickle Cell Disease
Randomized controlled trial comparing individual vs. weight based opioid protocols to treat VOE in EDs

• 1UG3/UH3 -HL137856-01 – NIH – NHLBI
  • Clinical Coordinating Center
  • PI – Paula Tanabe, PhD, RN
• Partner grant: U24 –
  • Data Coordinating Center - Awarded to the Duke Clinical Research Institute
  • PI – Huiman Barnhart, PhD

Based on NHLBI recommendations
AIMS

The primary objective of the COMPARE-VOE study is to compare change in pain scores from placement to study endpoint, in response to two different treatment regimens (weight based vs. individualized) for treating acute painful VOE in SCD.

- All patients will be followed for a maximum of 6 hours in the ED, or until time of placement in observation status, discharge or inpatient admission.

The secondary objectives of this study protocol will be the following endpoints:
- ED length of stay
- Hospitalization for pain control
- Return ED visits, hospitalizations or day hospital visits within seven days of the index ED visit
- Safety and side effects
Six Study Sites
Inclusion – Exclusion Criteria

**Inclusion Criteria**

- > 18 years of age
- SCD patients with the following genotypes:
  - Hgb SS, SC and SB+
  - SB- thalassemia

**Exclusion Criteria**

- Patients with sickle cell trait
- Patients with a treatment protocol that does not allow administration of opioids
- Patients with an existing ED protocol that includes oral opioids only
- Patients prescribed buprenorphine-containing medication in the outpatient setting
- Patients prescribed methadone
Study Flow Chart

Screen potential participants by inclusion and exclusion criteria for randomization population; obtain informed consent for up to 460 participants; randomize them to one of the two analgesic protocols; develop and upload the analgesic protocol in EMR.

Randomization Arm 1
Patient-specific analgesic protocol

Randomization Arm 2
Weight-based SCD specific protocol

Participant presenting to the ED for their visit due to VOE will be automatically enrolled to the study population with a target sample size of 230.

Perform first interview once participant is placed in a treatment area.

Once treatment is started, repeat interview every 30 minutes until the time of disposition (hospital admission, discharged home or assigned to observation status) or a maximum treatment duration of 6 hours, whichever comes first.
Procedures

- Patients are pre-enrolled in clinic or hospital for possible future ED visits for the treatment of VOE
- Randomized to receive either a patient specific (weight based) or individualized opioid treatment plan for VOE
- Plans are place in the HER
- EM provider to order analgesic plan
- Research staff will obtain baseline interview at ED treatment placement and q 30 minutes until endpoint (6 hours, DC home or decision to admit to hospital)
Interviews

- Pain scores directly from the patient
- Other satisfaction with pain questions
- Side effect assessment (itching, nausea)
- Safety
- Electronic health record review for administration of narcan and vasoactive medications, supplemental oxygen or intubation and vital signs
Study Status

As of July 2019

• X sites have been activated and are enrolling subjects
• X patients enrolled
• X ED study visits
• Anticipated enrollment completion: August 2021
• Planned study end: August 2022
Barriers to Care

- Chronic Pain and the Perception of Addiction
  - SCD Stigma
  - Racism
  - Clinician and Patient Knowledge Deficit
  - Frequent Visits
Adult Emergency Department Patients With Sickle Cell Pain Crisis: Results From a Quality Improvement Learning Collaborative Model to Improve Analgesic Management

Paula Tanabe, PhD, RN, MSN, MPH, John W. Hafner, MD, MPH, Zoran Martinovich, PhD, and Nicole Artz, MD

<table>
<thead>
<tr>
<th>Time period 2 years</th>
<th>Number of patients</th>
<th>Number of ED visits</th>
</tr>
</thead>
<tbody>
<tr>
<td>Site 1</td>
<td>88</td>
<td>959</td>
</tr>
<tr>
<td>Site 2</td>
<td>31</td>
<td>807</td>
</tr>
<tr>
<td>Site 3</td>
<td>212</td>
<td>1169</td>
</tr>
</tbody>
</table>

Among Medicaid patients, Sickle cell anemia ranked:

#1 as the most common principal diagnosis for re-admission rates within 30 days (34.4%)

#2 for re-admission within 7 days (9.8%)

High Prevalence of Social Behavioral Health Needs

- 147 ED patients with VOE interviewed within 2 weeks of an ED visit
- 20% reported anxiety
- 29% reported depression
- 11% prevalence of transportation
- 9% pharmacy
- 27% insurance challenges
- Care management can assist with these challenges

Discharge Home, Referrals

• Consult case management or social work early to identify unmet needs and work with patients with high numbers of ED visits or hospitalizations.

• All SCD patients can be screened for psychosocial needs in the ED

• Screen can be done by social worker, case manager, nurse or physician

• Screening form available at:
  http://sickleemergency.duke.edu/pain-and-case-management

• http://sickleemergency.duke.edu/sites/default/files/CM%20Referral%20Form.pdf
## Sickle Cell Disease Referral Form

Provide the following information for the sickle cell patient to be referred. Please inform the patient they will be contacted by CCNC to assist with the arrangement of additional resources if needed.

<table>
<thead>
<tr>
<th>Date of Referral from ED:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient Last Name:</td>
</tr>
<tr>
<td>Patient First Name:</td>
</tr>
<tr>
<td>Best contact info for patient: Name: Name: #:</td>
</tr>
<tr>
<td>2nd contact</td>
</tr>
<tr>
<td>Patient DOB:</td>
</tr>
<tr>
<td>Patient Medicaid ID:</td>
</tr>
<tr>
<td>Patient County of Residence</td>
</tr>
<tr>
<td>Referring ED:</td>
</tr>
<tr>
<td>Referring Provider, Credentials, contact</td>
</tr>
<tr>
<td>Patient is aware of referral</td>
</tr>
<tr>
<td>Primary Care Provider, if known</td>
</tr>
<tr>
<td>Sickle Cell Specialist, if known</td>
</tr>
<tr>
<td>Care Plan Attached: Yes or No</td>
</tr>
<tr>
<td>List Specific Reason for Referral (CHECK ALL THAT APPLY)</td>
</tr>
<tr>
<td>• Emotional</td>
</tr>
<tr>
<td>• Financial (Insurance, bills)</td>
</tr>
<tr>
<td>• Medical (Needs PCP)</td>
</tr>
<tr>
<td>• Prescriptions</td>
</tr>
<tr>
<td>• Relational Issues/Family Support System</td>
</tr>
<tr>
<td>• Transportation</td>
</tr>
<tr>
<td>• Pain Management</td>
</tr>
<tr>
<td>Additional Comments:</td>
</tr>
</tbody>
</table>

Please fax completed form to: CCNC Call Center: 888.978.0643

Form Completed By / Date:
Discharge Home, Analgesic Prescriptions, & Referrals

• FAX completed screening form to CCNC Call Center: one #
• Form will then be faxed to patient’s individual case manager
• CCNC is NC’s approach to managed care for persons with Medicaid
• CCNC will reach out to patient to help address needs identified on the screening form

OUTCOMES

• Over 900 referrals from EDs in NC have been made since 2014
• 98% are followed up within 3 days by CCNC
• The program can be adapted internally to your hospital
• Social behavioral health screening should occur in the in-patient setting as well
• Nurses are in a pivotal position to identify these needs and make referrals
Available to download in the Apple App Store for free.

Use password 1234 for general use or email Dr. Nirmish Shah at Nirmish.shah@duke.edu for specialty access
Disclosures

• R34
• R18 RHS024501A - Agency for Healthcare Research and Quality
• 1UG3/UH3 -HL137856-01 – NIH - NHLBI
• U01HL133964  - NIH, NHLBI

• Community Care of North Carolina
• North Carolina Emergency Nurses Association
Study Team
References


