Longitudinal Relationship Between Hydroxyurea Adherence and Health-related Quality of Life among Adolescents with Sickle Cell Disease

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Conflict of Interest

Grant/Research Support:

• Agency for Healthcare Research and Quality (AHRQ), NU-PATIENT K12 (PI)
• Northwestern University Clinical and Translational Sciences Institute (NUCATS) (PI)
• Pfizer ASPIRE Sickle Cell (PI)
• PCORI Implementation Research (Co-I)

Memberships:

• ASPHO / ASH, Pediatric Hematology Choosing Wisely Panel, Member
• ASH, Committee on Quality, Subcommittee on Stewardship, Member
• Journal of Medical Interest Research (JMIR) Pediatrics and Parenting, Editor-in-Chief
• U.S. Health Resources and Services Administration, Using Technology to Prevent Childhood Obesity in Low Income Families and Communities, Expert Panel Member
Objectives

• Review a brief background of sickle cell disease (SCD)

• Review the challenges of hydroxyurea adherence and the status of HRQOL in SCD.

• Preliminary data from an ongoing longitudinal study.

• Future directions.
The Challenge
Sickle cell disease is common in Blacks

- SCD is the most common genetic disorder in the USA, affecting about 100,000 Americans and 1 in 350 AA. (NHLBI; Hassell KL, 2010)
SCD is a devastating chronic illness

- Complications: pain, acute chest syndrome, pulmonary hypertension, stroke, end organ damage... (Rees et al, 2010)

- Patients have poor quality of life (QOL) (Panepinto and Bonner, 2012; Palermo T et al, 2002)

Images:
- Stroke
- Heart and Lung
- Unexpected Pain
- Fatigue and depression
Benefits of Hydroxyurea in SCD


SCD: sickle cell disease
Hydroxyurea is Safe in SCD

Ware RE. Blood 2010;115:5300-11

SCD: sickle cell disease
Hydroxyurea works for SCD patients

- HU Indications: Frequent pain or ACS, others... (Yawn et al, 2014)


- Adherence remains suboptimal (40-50%). (Walsh et al, 2014)
The Challenge
Sickle Cell Disease

Healthcare Utilization

Hydroxyurea Adherence

Barriers

Perceptions

Quality of Life

Mobile Technology Interventions

Mobile App

NU-PATIENT K12

AHRQ
Agency for Healthcare Research and Quality

HUGo

NORTHWESTERN UNIVERSITY
Behavior Change Wheel (COM-B)
Study Objective

- To Assess the longitudinal relationship of HU adherence to stakeholder selected HRQoL domains, including fatigue and depression, and other patient-reported outcomes.

- **Hypothesis 2**: Low HU adherence is associated with impairment of HRQoL domains.
Study Methods

• Outpatient SCD clinic

• Eligibility Criteria:
  o SCD (all genotypes)
  o On hydroxyurea
  o 8 years and older
  o English-speaking

Hydroxyurea Adherence (subjective and objective)

HRQOL (PROMIS and PedsQL)

Other Important PROs

SCD: sickle cell clinic
Adherence Outcomes

- Clinical Effects
- Surveys
- Biological markers

- Medication Possession Ratio (MPR)
- Electronic Pill Bottle
Study Measures

- HRQOL
  - PROMIS measures
  - PedsQL
- Other PROs
  - Brief medication questionnaire (barriers)
  - Brief illness perceptions questionnaire
  - Treatment satisfaction questionnaire
  - Sickle cell stigma
Enrollment

• Total of 28 dyads / participants:
  o 28 completed visit 1 (Baseline)
  o 19 completed visit 2 (3-4 month)
  o 12 completed visit 3 (6 month)
  o 3 completed visit 4 (9 month)
  o 1 completed visit 5 (12 month)
## Participants Characteristics

<table>
<thead>
<tr>
<th>Patients</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (years)</td>
<td>16.4 ± 3</td>
</tr>
<tr>
<td>Females</td>
<td>62%</td>
</tr>
<tr>
<td>Black or African American</td>
<td>100%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Parents</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean ± SD (years)</td>
<td>41.2 ± 5.3</td>
</tr>
<tr>
<td>Females</td>
<td>93%</td>
</tr>
</tbody>
</table>
## HU Adherence – Patients

<table>
<thead>
<tr>
<th>Measures</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS, mean ± SD</td>
<td>72 ± 21</td>
</tr>
<tr>
<td>VAS (&lt;90%)</td>
<td>69%</td>
</tr>
<tr>
<td>MMAS-8, mean ± SD</td>
<td>4.7 ± 1.8</td>
</tr>
<tr>
<td>MMAS-8 (Low &lt;6)</td>
<td>69%</td>
</tr>
<tr>
<td>MMAS-8 (Low / Moderate)</td>
<td>100%</td>
</tr>
</tbody>
</table>
## HU Adherence – Parents

<table>
<thead>
<tr>
<th>Measures</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>VAS, mean ± SD</td>
<td>85.3 ± 15.6</td>
</tr>
<tr>
<td>VAS (&lt;90%)</td>
<td>53%</td>
</tr>
<tr>
<td>MMAS-8, mean ± SD</td>
<td>5.7 ± 1.1</td>
</tr>
<tr>
<td>MMAS-8 (Low &lt;6)</td>
<td>40%</td>
</tr>
<tr>
<td>MMAS-8 (Low / Moderate)</td>
<td>73%</td>
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</tbody>
</table>
# HU Adherence Barriers - Patients

## Barriers and Adherence Rates

<table>
<thead>
<tr>
<th>Barriers</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative beliefs</td>
<td>44%</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>56%</td>
</tr>
<tr>
<td>Access barrier</td>
<td>31%</td>
</tr>
<tr>
<td>Endorsed any barrier</td>
<td>69%</td>
</tr>
<tr>
<td>Endorsed ≥ 1 barrier</td>
<td>50%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Barriers and Adherence Rates</th>
<th>R</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMAS</td>
<td>-0.79</td>
<td>0.003</td>
</tr>
<tr>
<td>VAS</td>
<td>-0.7</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
HU Adherence Barriers - Parents

<table>
<thead>
<tr>
<th>Barriers</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Negative beliefs,</td>
<td>19%</td>
</tr>
<tr>
<td>Forgetfulness</td>
<td>25%</td>
</tr>
<tr>
<td>Access barrier</td>
<td>38%</td>
</tr>
<tr>
<td>Endorsed any barrier</td>
<td>63%</td>
</tr>
<tr>
<td>Endorsed ≥ 1 barrier</td>
<td>19%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Barriers and Adherence Rates</th>
<th>R</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>MMAS</td>
<td>-0.39</td>
<td>0.14</td>
</tr>
<tr>
<td>VAS</td>
<td>-0.36</td>
<td>0.17</td>
</tr>
</tbody>
</table>
Other PROs - Patients

- 92% overall satisfied with hydroxyurea as a treatment option

- Perceptions of hydroxyurea varied and were not significantly correlated with adherence rates

- About 38% endorsed stigma related to SCD

- Higher stigma score was associated with lower adherence rates
  - MMAS: $R = -0.5$, $P$-value 0.04
  - VAS: $R = -0.49$, $P$-value 0.05
Other PROs - Parents

- 87% overall satisfied with hydroxyurea as a treatment option
- Perceptions of hydroxyurea varied
- About 46% endorsed stigma related to SCD
- Stigma score was not correlated with adherence rates
## PROMIS Measures (T-scores)

<table>
<thead>
<tr>
<th>Domains, Median (IQR)</th>
<th>Patients</th>
<th>Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fatigue</td>
<td>56.5 (45.5 – 62.2)</td>
<td>48.4 (37.9 – 65.8)</td>
</tr>
<tr>
<td>Pain Behavior</td>
<td>42.5 (23.9 – 52.9)</td>
<td>27.7 (17.5 – 55.1)</td>
</tr>
<tr>
<td>Pain Interference</td>
<td>42.6 (32 – 62.6)</td>
<td>51.6 (36.8 – 64.2)</td>
</tr>
<tr>
<td>Mobility</td>
<td>47.8 (44.2 – 52.1)</td>
<td>45.9 (37.5 – 51.9)</td>
</tr>
<tr>
<td>Physical Activity</td>
<td>47.1 (37.6 – 49.2)</td>
<td>47.9 (42.8 – 53.4)</td>
</tr>
<tr>
<td>Phys Stress Sx</td>
<td>62.3 (54.2 – 66.1)</td>
<td>60.7 (52.5 – 68.5)</td>
</tr>
<tr>
<td>Psych Stress Sx</td>
<td>54.9 (46.2 – 60.8)</td>
<td>50.2 (40.4 – 61.3)</td>
</tr>
<tr>
<td>Depression</td>
<td>52.8 (37.8 – 55.8)</td>
<td>46.9 (32.1 – 57.6)</td>
</tr>
<tr>
<td>Anxiety</td>
<td>44.4 (36.4 – 54.2)</td>
<td>50.7 (41.1 – 57)</td>
</tr>
</tbody>
</table>
PROMIS Measures (T-scores)...

<table>
<thead>
<tr>
<th>Domains, Median (IQR)</th>
<th>Patients</th>
<th>Parents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Social Isolation</td>
<td>41.8 (34.6 – 49.7)</td>
<td>42.6 (39.7 – 46.8)</td>
</tr>
<tr>
<td>Cognitive Function</td>
<td>50.3 (44.7 – 55.3)</td>
<td>49.7 (42.5 – 55.7)</td>
</tr>
<tr>
<td>Positive Affect</td>
<td>46.4 (37.4 – 52.9)</td>
<td>48.6 (42.5 – 52.7)</td>
</tr>
<tr>
<td>Meaning and Purpose</td>
<td>46.6 (35.4 – 51.4)</td>
<td>52.5 (43.9 – 56)</td>
</tr>
<tr>
<td>Life Satisfaction</td>
<td>43.8 (36.6 – 49.7)</td>
<td>44.1 (39.3 – 51.9)</td>
</tr>
<tr>
<td>Self-Efficacy Meds</td>
<td>42.9 (38.5 – 45)</td>
<td>----</td>
</tr>
<tr>
<td>Self-Efficacy Sx Management</td>
<td>46.3 (44.3 – 49.3)</td>
<td>45 (41.6 – 49.3)</td>
</tr>
</tbody>
</table>
## HU Adherence and HRQOL – Patients

<table>
<thead>
<tr>
<th>Correlations</th>
<th>VAS</th>
<th>P-value</th>
<th>MMAS-8</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pain Interference</td>
<td>-0.57</td>
<td>0.02</td>
<td>-0.51</td>
<td>0.04</td>
</tr>
<tr>
<td>Psych Stress Symptoms</td>
<td>-0.66</td>
<td>0.005</td>
<td>-0.74</td>
<td>0.001</td>
</tr>
<tr>
<td>Depression</td>
<td>-0.63</td>
<td>0.01</td>
<td>-0.67</td>
<td>0.005</td>
</tr>
<tr>
<td>Anxiety</td>
<td>-0.5</td>
<td>0.04</td>
<td>-0.48</td>
<td>0.06</td>
</tr>
<tr>
<td>Social Isolation</td>
<td>-0.46</td>
<td>0.07</td>
<td>-0.41</td>
<td>0.11</td>
</tr>
<tr>
<td>Self-Efficacy Medications</td>
<td>0.45</td>
<td>0.08</td>
<td>0.53</td>
<td>0.03</td>
</tr>
</tbody>
</table>

- There was no significant correlation between parents’ report of HRQOL or PROs and HU adherence rates using VAS or MMAS-8.
Positive Thoughts about Hydroxyurea

- Parents:
  - “I think it is a very positive medicine for SCD, if it is taken consistently we will not have too many crisis”
  - “Since taking this medication my child has less sickle cell issues”
  - “It's a miracle medicine, we are so thankful for this option”

- Patients:
  - “It has helped me to feel better and get stronger, and not be sick”
  - “It helps with my future”
  - “Always getting right dose and I'm not experiencing any side effects”
Negative Thoughts about Hydroxyurea

• Parents:
  o “Copay, refrigerated, only in Chicago pharmacy, taste”
  o “Need better flavors”
  o “Taking it for the rest of ones life”

• Patients:
  o “Bad taste and the pills are to big”
  o “I feel like it doesn't really work”
  o “It is very hard to take as many as I have to take”
Conclusions

• Low hydroxyurea adherence rates were common among patients with SCD and their parents.

• Patients and parents reported various barriers to hydroxyurea adherence.

• Participants with fewer barriers to hydroxyurea adherence and more favorable PROs, were more likely to have higher adherence rates.

• Routine assessment of hydroxyurea adherence, its related barriers and HRQOL or PROs could provide actionable information to improve adherence rates and other important clinical outcomes.
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Northwestern University

Zeinab Alward
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Questions

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