Newborn Screening in the NICU: Colorado's Experience with Screening Low Birth Weight Infants

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Objectives

• Goals of the project
• Compare the procedures outlined in the 2009 CLSI document NBS03-A “Newborn Screening for Preterm, Low Birth Weight, and Sick Babies: Approved Guidelines” to procedures outlined in Colorado’s Rules and Regulations.

• Methods
• Results
• Conclusions
• Next Steps
Goals

• Perform a baseline evaluation of newborn screening results in the NICU population of Colorado
  – Timing of first specimen collection
  – First NBS obtained before or after blood transfusion
  – Differences in timing of screening in study population as compared to all CO screening and across categories of interest
  – Rate and type of abnormal screening results
  – Regulatory or protocol changes to improve NBS for NICU population

• Conducted as a master’s degree capstone project of Genetic Counseling graduate student Jeanine Ashley
Comparison

CLSI 2009 Guidelines

- Screening protocols should be different for newborns requiring intensive care
- Goal: NBS in shortest time, with highest reliability, and fewest specimens
- Recommended 3-step protocol for screening NICU population
- First screen upon admission to NICU, unless already done
- Second screen at 48-72 hours of life if:
  - First screen was before 24 hours
  - Weight was less than 2000g at birth
  - Abnormal results on first screen
- Third screen at 28 days or upon discharge

Colorado Rules and Regulations

- All infants treated the same with exception of transfused infants for collection.
- Specimens are to be collected prior to blood transfusion, if applicable.
- First screening specimen: as late as possible prior to discharge but no later than 48 hours after birth
- Second screening specimen: 8 to 14 days old
- Weight dependent cut-offs for CAH. Follow-up protocols accommodate for TPN.
Methods

• Data query
  – Colorado NBS laboratory demographics and results data extracted from Specimen Gate®.
  – De-identified
  – Three years: 2012-2014
  – Birth weight, age at first NBS collection, blood transfusion status, screening facility, and results.

• Target population: newborns in CO NICUs
  – Birth weight of 1800g or less used as proxy as NICU status was not collected as a demographic on the NBS card.
  – Compare NICU data to aggregate data of Colorado’s population
Methods: data stratification

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>Category name</th>
</tr>
</thead>
<tbody>
<tr>
<td>400g – 999g</td>
<td>Extremely low birth weight (ELBW)</td>
</tr>
<tr>
<td>1000g – 1499g</td>
<td>Very low birth weight (VLBW)</td>
</tr>
<tr>
<td>1500g – 1800g</td>
<td>Low birth weight (LBW)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Time of collection</th>
<th>Category name</th>
</tr>
</thead>
<tbody>
<tr>
<td>No entry, -5.05 hrs, 0 hrs</td>
<td>Missing</td>
</tr>
<tr>
<td>&gt; 0 to &lt; 24 h</td>
<td>Early</td>
</tr>
<tr>
<td>24 h to &lt; 48 h</td>
<td>On time</td>
</tr>
<tr>
<td>48 h to &lt; 72 h</td>
<td>Late</td>
</tr>
<tr>
<td>72 h to &lt; 300 h</td>
<td>Very late</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Facility category</th>
<th>Description</th>
<th>No. of facilities</th>
</tr>
</thead>
<tbody>
<tr>
<td>Level I</td>
<td>Well-baby nursery</td>
<td>10</td>
</tr>
<tr>
<td>Level II</td>
<td>Special Care nursery</td>
<td>15</td>
</tr>
<tr>
<td>Level III</td>
<td>NICU</td>
<td>16</td>
</tr>
<tr>
<td>Level IV</td>
<td>Regional NICU</td>
<td>2</td>
</tr>
</tbody>
</table>
Summary of Data

- 4076 records evenly split over 3 years

Mean birth weight 1340g

Distribution of screening among Nursery Level

- LBW
- VLBW
- ELBW

- Level I
- Level II
- Level III
- Level IV
Timing of NBS: NICU vs. All CO Newborns

Study population vs. All CO Newborns:

- **Early**
  - Study population: 5%
  - All CO Newborns: 10%

- **On Time**
  - Study population: 75%
  - All CO Newborns: 80%

- **Late**
  - Study population: 20%
  - All CO Newborns: 5%

- **Very Late**
  - Study population: 0%
  - All CO Newborns: 0%
## Blood transfusion status

<table>
<thead>
<tr>
<th>Transfused prior to screening?</th>
<th>Frequency</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>117</td>
<td>2.9%</td>
</tr>
<tr>
<td>No</td>
<td>3700</td>
<td>90.8%</td>
</tr>
<tr>
<td>Unknown</td>
<td>259</td>
<td>6.3%</td>
</tr>
</tbody>
</table>
Abnormal Screening Results

• 1372 (not investigated for overlap)
  – Amino acidemias (all 8)
  – Organic acidemias (9 of 11)
  – Fatty acid oxidation disorders (5 of 10)
  – Endocrinopathies
  – Hemoglobinopathies
  – Cystic fibrosis
  – Severe Combined Immunodeficiency)

• True positives? 4
  – Congenital Hypothyroidism
## Positive Predictive Values

<table>
<thead>
<tr>
<th>Disorders</th>
<th>Study population: ≤1800g</th>
<th>Newborns &gt;1800g</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ABN</td>
<td>TP</td>
</tr>
<tr>
<td><strong>Amino Acid Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>ARG</td>
<td>223</td>
<td>0</td>
</tr>
<tr>
<td>CIT/ASA</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>HCY/MET</td>
<td>407</td>
<td>0</td>
</tr>
<tr>
<td>MSUD</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>PKU/HyperPHE</td>
<td>43</td>
<td>0</td>
</tr>
<tr>
<td>Tyrosinemias</td>
<td>137</td>
<td>0</td>
</tr>
<tr>
<td><strong>Fatty Acid Oxidation</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disorders</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CPTI</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>CUD</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>MCADD</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>SCADD</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td><strong>Organic Acid Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>C5OH disorders</td>
<td>8</td>
<td>0</td>
</tr>
<tr>
<td>BIOT</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>GA1</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>GA2</td>
<td>32</td>
<td>0</td>
</tr>
<tr>
<td>IVA</td>
<td>36</td>
<td>0</td>
</tr>
<tr>
<td>MAL</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>PA/MMA</td>
<td>27</td>
<td>0</td>
</tr>
<tr>
<td><strong>Endocrine Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CAH</td>
<td>86</td>
<td>0</td>
</tr>
<tr>
<td>CH</td>
<td>44</td>
<td>4</td>
</tr>
<tr>
<td><strong>Other Disorders</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CF</td>
<td>88</td>
<td>0</td>
</tr>
<tr>
<td>Hemoglobinopathy</td>
<td>163</td>
<td>0</td>
</tr>
<tr>
<td>SCID</td>
<td>26</td>
<td>0</td>
</tr>
</tbody>
</table>
Abnormal screening results: study population vs. newborns over 1800g

- SCID ≤ 1800g: 36.6%, > 1800g: 35.5%
- Inborn Errors Metabolism: ≤ 1800g: 35.5%
- Endocrine Disorders: ≤ 1800g: 8.8%
- Cystic Fibrosis: ≤ 1800g: 3.6%
- Hemoglobinopathies: ≤ 1800g: 2.2%
- Population Proportion: ≤ 1800g: 2.1%
Discussion: Collection Time

• Early screening not worrisome for NICU population as the need to screen before transfusion.
• Late screening (> 48 hours) for 28.8% of the NICU population as compared to 6% of all CO newborns.
  – Risk for screening impacted by treatments
  – Risk for late identification of disorders
  – Risk for false negatives of disorders (FAO disorders)
• Missing information: no time of collection entered for 581 newborns during study period (14.3%)
• Gap noted: for transferred infants, screening responsibility not defined by CO’s rules and regulations.
Discussion: Blood Transfusion

• 117 infants screened after transfusion
  – Risk of false negatives

• Missing information for 6.3%
  – Don’t know the blood transfusion status

• Clinical judgement prevails:
  – Likely to be a small number of infants with screening after transfusion

• Gap noted: No system in place for following up with the transfused infants nor no guidance provided on reports for risks and need for repeat screening.
Discussion: Abnormal Results

• NICU population requires a disproportionate amount of NBS follow-up efforts
  – Amino acidemias: TPN
  – Fatty acid oxidation: carnitine, MCT, transfusion
  – Organic acid disorders: antibiotics, hyperbilirubinemia
  – Endocrinopathies: prematurity
  – Cystic fibrosis: prematurity, stress
  – Hemoglobinopathies: transfusion
  – SCID: transfusion, prematurity

• Gap noted: Minimal information on NBS collection card to assist lab with interpretation of results
  – Other states include gestational age, type of feeding, antibiotics, hyperbilirubinemia on collection card
Conclusion

• Results illustrated gaps in the Colorado NBS system.
  • Late screening was significantly higher for NICU population
  • No guidance for transfused infants
  • Screening responsibility of transferred infants not defined

• Results demonstrated the burden that NICU populations places on the NBS system.
  – Study population represented disproportionate number of abnormal screening results
  – False positives comprise the vast majority of abnormal screening results for this population
Next Steps

• Revised NBS cards in December 2015
  – NICU status (Y/N)
  – Reason not screened
    • Deceased
    • Transferred (and to what facility)
    • Refused
    • Other

• Updates underway for Specimen Gate®
  – Tracking of the new fields with appropriate queries
  – Improved guidance for follow-up of transfused infants
...Next Steps

• Improving NICU educational efforts
  – NICU specific report cards for larger NICU facilities to be created
  – NICU educational presentations scheduled for 2016

• Rules and Regulations changes proposed for 2016
  – Improve language regarding collection
  – Require submission of NBS card for all infants even if not screened
  – Define responsibility for screening of transferred infant
Acknowledgements

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