Shortened IV antibiotic courses for infant group B Streptococcal bacteremia

Eric Coon, MD, MS
Raj Srivastava, MD, MPH
Greg Stoddard, MS
Samir Shah, MD, MSCE

Eric Coon has documented no financial relationships to disclose or Conflicts of Interest (COIs) to resolve.
Background

- Late onset GBS disease: 1/3,000 infants\(^1\)
- Red Book ➔ Minimum 10 days IV therapy
- PICC complications are frequent\(^2\)
- Oral antibiotics ➔ Bactericidal levels\(^3\)
- Environmental influences on recurrence\(^4-6\)
- Efficacy of early oral therapy for serious disease\(^7-9\)

\(^1\) Phares et al. *JAMA*. 2008 May.

Objective

Among infants with late onset uncomplicated GBS bacteremia admitted to US children’s hospitals:

1. Determine the prevalence of shortened IV antibiotic therapy prescriptions
2. Compare outcomes for infants receiving prolonged vs. shortened IV antibiotic therapy
Methods

- Retrospective cohort
- Pediatric Health Information System (PHIS) database
  - De-identified patient demographic data
  - ICD-9 diagnosis and procedure codes
  - Laboratory, imaging, pharmacy, and supply charges
- Between Jan 2000-Sept 2015

Inclusion Criteria

1. GBS disease
   41.02 streptococcus infection, Group B
   AND
2. Bacteremia
   38.0 streptococcal septicemia
   38.9 unspecified septicemia
   790.7 bacteremia
Exclusions (index visit)

- Meningitis, osteomyelitis, non-GBS bacteremia, or HSV
- Age <7 days or >4 months
- Gestational age <29 weeks or birth weight <1500 grams
- PICU or NICU stay
- Hospitalization >14 days
- Transferred out of PHIS hospital

Exposure

Receipt of a shortened course of IV antibiotic therapy

- discharge from the index GBS visit after a length of stay ≤ 8 days, without a charge for a PICC
Patient Outcomes

Recurrence
- hospital revisit for GBS bacteremia, meningitis, or osteomyelitis in the first year of life

Treatment Failure
- hospital revisit for GBS bacteremia, meningitis, or osteomyelitis within 14 days of discharge

Statistical Analysis

- Propensity scores computed with multivariable logistic regression, using:
  - Gender
  - Age
  - Race/ethnicity
  - Insurance payer
  - Gestational age
  - Complex chronic condition presence
  - Hospital level case mix index
  - Admission year

- Patients then weighted by the inverse of their propensity (IPW)
- Adjusted, weighted regression analysis
Validation of codes

- Receipt of PICC\(^1\)
  - PICC PPV=85%
  - PICC NPV=99%
- Diagnosis of GBS bacteremia (Utah data)
  - Sensitivity= 23/32 (72%)
  - PPV=23/24 (96%)

\(^1\)Samir Shah, personal communication, June 30, 2017.

Flowchart of study cohort

1,369 Infants ≤ 4 months of age discharged between January 1, 2000-October 1, 2015
with GBS bacteremia from 49 children's hospitals

594 Excluded
- 122 concomitant non-GBS bacteremia or HSV
- 37 age <7 days
- 16 gestational age <29 weeks or birth weight <1500 grams
- 249 meningitis or osteomyelitis
- 61 hospitalization >14 days or transferred out
- 109 PICU or NICU stay

775 uncomplicated, late-onset GBS bacteremia

- 612 Prolonged IV therapy
- 163 Shortened IV therapy
Proportion of children at each hospital who received a shortened IV course

Cohort characteristics

<table>
<thead>
<tr>
<th></th>
<th>Shortened IV therapy N=163</th>
<th>Prolonged IV therapy N=612</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female</td>
<td>81 (50)</td>
<td>289 (47)</td>
<td>0.58 a</td>
</tr>
<tr>
<td>Age, n (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-30 days old</td>
<td>13 (8)</td>
<td>80 (13)</td>
<td>&lt;0.01 b</td>
</tr>
<tr>
<td>31-90 days old</td>
<td>124 (76)</td>
<td>475 (78)</td>
<td></td>
</tr>
<tr>
<td>&gt;90 days old</td>
<td>26 (16)</td>
<td>57 (9)</td>
<td></td>
</tr>
<tr>
<td>Race/Ethnicity</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>White Non-Hispanic</td>
<td>62 (38)</td>
<td>215 (35)</td>
<td></td>
</tr>
<tr>
<td>Black Non-Hispanic</td>
<td>59 (36)</td>
<td>251 (41)</td>
<td>0.74 a</td>
</tr>
<tr>
<td>Hispanic</td>
<td>23 (14)</td>
<td>81 (13)</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>19 (12)</td>
<td>65 (11)</td>
<td></td>
</tr>
<tr>
<td>Primary payer</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Government</td>
<td>111 (68)</td>
<td>367 (60)</td>
<td>0.08 a</td>
</tr>
<tr>
<td>Commercial insurance/self-pay</td>
<td>41 (25)</td>
<td>172 (28)</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>11 (7)</td>
<td>73 (12)</td>
<td></td>
</tr>
<tr>
<td>History of Prematurity</td>
<td>1 (1)</td>
<td>16 (3)</td>
<td>0.12 a</td>
</tr>
<tr>
<td>Complex Chronic Condition</td>
<td>19 (12)</td>
<td>63 (10)</td>
<td>0.62 a</td>
</tr>
<tr>
<td>Case Mix Index , median (IQR)</td>
<td>1.03 (0.99-1.04 (1.00-1.04)</td>
<td>1.11</td>
<td>0.52 a</td>
</tr>
<tr>
<td>Admission Year, median (IQR)</td>
<td>2007 (04-12)</td>
<td>2009 (05-12)</td>
<td>&lt;0.02 a</td>
</tr>
</tbody>
</table>

Unless otherwise noted, data are presented as number (percentage) of patients

a Chi-square
b Wilcoxon Mann Whitney (WMW)
c t-test
Length of stay distribution, among shortened courses

![Graph showing length of stay distribution]

Patient Outcomes

<table>
<thead>
<tr>
<th></th>
<th>Shortened</th>
<th>Prolonged</th>
<th>Relative effect (95% CI)</th>
<th>Absolute difference (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any Recurrence, n (%)</td>
<td>3 (1.8)</td>
<td>14 (2.3)</td>
<td>OR= 0.9 (0.2 to 3.6)*</td>
<td>-0.1% (-3.0 to 2.7%)*</td>
</tr>
<tr>
<td>Bacteremia</td>
<td>3 (1.8)</td>
<td>14 (2.3)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meningitis</td>
<td>1 (0.6)</td>
<td>1 (0.2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteomyelitis</td>
<td>0</td>
<td>0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Days to recurrence, b mean (SEM)</td>
<td>28 (15)</td>
<td>24 (8)</td>
<td>Coeff= 0.03 (-0.04 to 0.10)</td>
<td>9 (-13 to 31) c</td>
</tr>
<tr>
<td>Treatment Failure, n (%)</td>
<td>1 (0.6)</td>
<td>6 (1.0)</td>
<td>OR= 0.6 (0.1 to 5.5) a</td>
<td>-0.3% (-1.8 to 1.1%) a</td>
</tr>
</tbody>
</table>

* Odds ratio, obtained from propensity adjusted, inverse probability weighted logistic regression model
b Descriptive statistics using n=17 patients with recurrence
c Ratio of means, obtained from propensity adjusted, inverse probability weighted gamma regression model
Limitations

- Observational design
  - Unmeasured confounding
- PHIS database
  - Generalizability
  - Misclassification
- Rare outcomes
  - Limited power

Conclusions

- Shortened IV courses appear to be common
- Rates of recurrence and treatment failure appear to be low