

Shortened IV antibiotic courses for infant group B Streptococcal bacteremia

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



Background

- Late onset GBS disease: 1/3,000 infants¹
- Red Book → Minimum 10 days IV therapy
- PICC complications are frequent²
- Oral antibiotics → Bactericidal levels³
- Environmental influences on recurrence⁴⁻⁶
- Efficacy of early oral therapy for serious disease⁷⁻⁹

¹ Phares et al. *JAMA*. 2008 May.

² Jumani et al. *JAMA Pediatr*. 2013 May.

³ Gras-Le Guen. *Eur J Clin Pharmacol*. 2007 Jul.

⁴ Paredes et al. *J Pediatr*. 1976 Aug.

⁵ Hansen et al. *J Clin Microbiol*. 2004 Jan.

⁶ Filleron et al. *Arch Dis Child Fetal Neonatal Ed*. 2014 Jan.

⁷ Shah et al. *Pediatrics*. 2016 Dec.

⁸ Rangel et al. *Ann Surg*. 2016 Jul.

⁹ Keren et al. *JAMA Pediatr*. 2015 Feb.

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 \leq 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 PICC¹
 - PICC PPV=85%
 - PICC NPV=99%
- Diagnosis of GBS bacteremia (Utah data)
 - Sensitivity= 23/32 (72%)
 - PPV=23/24 (96%)

¹Samir Shah, personal communication, June 30, 2017.
From study: Shah et al. Pediatrics. 2016 Dec.



Flowchart of study cohort

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

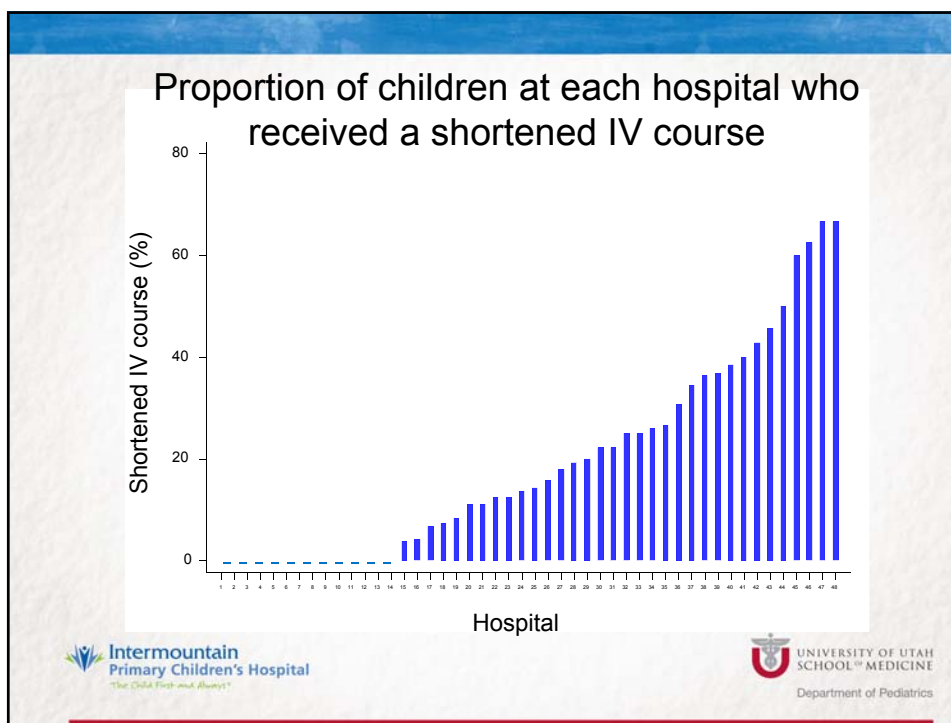
594 Excluded

- 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



Cohort characteristics

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

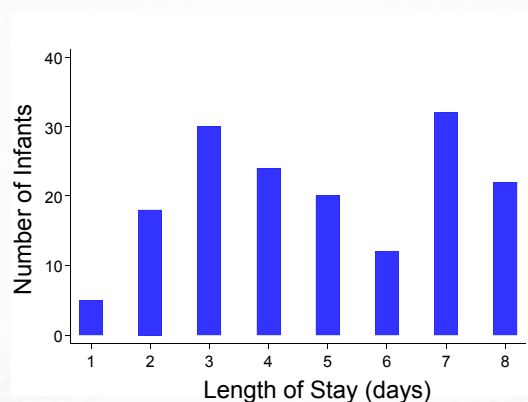
Unless otherwise noted, data are presented as number (percentage) of patients

a Chi-square

b Wilcoxon Mann Whitney (WMW)

c t-test

Length of stay distribution, among shortened courses



Patient Outcomes

	Shortened N=163	Prolonged N=612	Relative effect (95% CI)	Absolute difference (95% CI)
Any Recurrence, n (%)	3 (1.8)	14 (2.3)	OR= 0.9 (0.2 to 3.6) ^a	-0.1% (-3.0 to 2.7%) ^a
Bacteremia	3 (1.8)	14 (2.3)		
Meningitis	1 (0.6)	1 (0.2)		
Osteomyelitis	0	0		
Days to recurrence,^b mean (SEM)	28 (15)	24 (8)	Coeff= 0.03 (-0.04 to 0.10) ^c	9 (-13 to 31) ^c
Treatment Failure, n (%)	1 (0.6)	6 (1.0)	OR= 0.6 (0.1 to 5.5) ^a	-0.3% (-1.8 to 1.1%) ^a

^a 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