Uncomplicated Late-Onset Group B Streptococcal Bacteremia: Can We Do Less Than 10 Days IV?

Charles R. Woods, MD, MS

Late-onset group B streptococcal (LO-GBS) bacteremia remains a common serious infection in early infancy. It can be associated with meningitis, osteomyelitis, or other focal sites of infection but often occurs as uncomplicated bloodstream infection. Current authoritative sources recommend 10 days of intravenous (IV) antimicrobial therapy for uncomplicated LO-GBS bacteremia.[1,2] In this issue of *Pediatrics*, Coon et al[3] report an observational, comparative effectiveness study that revealed no difference in group B streptococcus (GBS) recurrence risk in young infants treated with shortened IV courses (≤8 days of IV therapy) versus prolonged courses (>8 days) for uncomplicated bacteremia.

We know that 10 days IV works well for this infection and is effective and safe, right? So, why wrestle with questions about duration of therapy? With a growing literature on potential impacts of antimicrobial therapy on the infant microbiome that may matter later in life, risks of antimicrobial resistance, risks associated with hospitalization in general, financial and social burdens of hospitalizations on families, and well-described IV catheter-associated risks during home IV therapy, addressing this question is reasonable. A place to start is, "How did we come to recommendations of 10 days of IV therapy for this entity?"

In his 1990 review of recommended durations of antimicrobial therapy for bacterial meningitis in children, Radetsky[4] stated, "…the standards for duration of treatment in meningitis have been more the distillations of clinical experience than the fruit of scientific study." The same still can be said for recommended durations of therapy for many bacterial infections, including uncomplicated LO-GBS bacteremia. In their 2014 review of evidence on this topic, Schroeder and Ralston[5] noted, "…to our knowledge there are no experimental or observational investigations to support this recommendation."

Red Book recommendations for antimicrobial therapy for uncomplicated LO-GBS bacteremia have changed slightly over the past 4 decades from "10 to 14 days" IV in the 1980s[6] to "at least 10 days" in the mid-1990s[7] to "10 days" since 2000.[8] Similarly, Pannaraj and Baker,[2] in the 2019 (eighth) edition of Feigin and Cherry's *Textbook of Pediatric Infectious Diseases*, recommend 10 days IV with this statement: "A shorter duration has not been documented to be efficacious, and relapses, though rare, have been reported in these circumstances." This language dates to the fourth edition in 1998.[9] The referenced recurrent cases received 10 days of IV therapy.[10,11]

Coon et al[3] assembled a cohort of 775 infants (163 shortened course, 612 prolonged course) between 7 days and 4 months of age who had uncomplicated courses of LO-GBS bacteremia using the Pediatric Health Information System database from 2000 to 2015. Premature infants born at <29 weeks' gestation or birth

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weight <1500 g were excluded, as were those with hospitalization >14 days or receipt of intensive care. The primary outcome was recurrence of GBS disease during the first year of life. Shortened-course infants were slightly older on average and had a few more concomitant urinary tract infections.[3]

Risk of recurrence of GBS infection among all 775 was 2.2%, or ~1 in 45. Duration of IV antimicrobial therapy, defined dichotomously, did not alter this risk. The adjusted risk difference was −0.2%, 95% confidence interval −3.0% to 2.5%. In the shortened IV group, >50% received ≤5 days of IV therapy, and at least 17% likely received additional oral antimicrobial therapy after discharge. In the prolonged IV group, 200 were deemed as going home with a peripherally inserted central catheter to complete a longer course, although their total IV durations were unknown.[3]

An important unknown factor is the possible role of oral antimicrobial therapy in the shortened IV group. Outpatient data are not available in the Pediatric Health Information System database. High-dose oral amoxicillin regimens (200–300 mg/kg per day) can generate therapeutic serum concentrations in term neonates with early onset GBS disease,[12] so any oral therapy added to initial IV therapy potentially could have contributed to the similarity of outcomes between the shortened versus prolonged IV groups.

What then should one conclude from this study by Coon et al[3]? The broad answer is that, for uncomplicated LO-GBS bacteremia, ≤8 days of IV therapy appears to carry a risk of recurrent GBS infection that is not different from >8 to 10 days IV. The −0.2% point estimate favoring shortened IV courses generates a number needed to treat of 500 to prevent 1 recurrent GBS case with prolonged IV courses.[3] These are encouraging data that will provide some with enough comfort to select IV courses <10 days, whereas others will remain unconvinced.

For those ready to adopt shorter IV courses for uncomplicated LO-GBS bacteremia, a number of practical questions remain. For example, is a 5-day IV course as safe as 7 or 8 or 10 days, with any risks truly balanced by the potential complications of longer IV therapy? Should shortened IV courses be supplemented with oral therapy to complete a total course of 10 days? Should a 2-week-old infant be viewed the same as an 8-week-old infant? This study is a good step forward but cannot help us with these and other similar questions. We still must struggle to weigh courage against wisdom.

What are the next steps? We are unlikely to see randomized controlled trials to answer this and similar questions any time soon. To make progress, we may have to learn to overcome "academic imprinting," where we tend to demand a far greater level of evidence (eg, randomized controlled trials) to overturn long-standing practices taught during our training years but which often are based on far lesser levels of evidence (eg, case series, first principles data).

A middle ground can be high-quality comparative effectiveness studies, as provided by Coon et al.[3] Further progress requires more robust databases (ie, with more inpatient and outpatient diagnostic and therapeutic data elements) coupled with multicenter multidisciplinary consensus-based best-practice protocols. The iterative analyses that would then be possible could provide guidance toward antimicrobial courses that are long enough, but not too long. Identifying biomarkers that correspond sufficiently with control of infection to allow safe discontinuation of antimicrobial therapies will also help.

ABBREVIATIONS

GBS: group B streptococcal
IV: intravenous
LO-GBS: late-onset group B streptococcal

REFERENCES

1. Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018-2021 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics; 2018
2. Pannaraj PS, Baker CJ. In: Cherry RD, Harrison GJ, Kaplan SL, Steinbach WJ, Hotez PJ, eds. *Feigin and Cherry's Textbook of Pediatric Infectious Diseases*, 8th ed. Philadelphia, PA: Elsevier; 2019:832–834
3. Coon ER, Srivastava R, Stoddard G, Wilkes J, Pavia AT, Shah SS. Shortened IV antibiotic course for uncomplicated, late-onset group B streptococcal bacteremia. *Pediatrics*. 2018;142(5):e20180345
4. Radetsky M. Duration of treatment in bacterial meningitis: a historical inquiry. *Pediatr Infect Dis J*. 1990;9(1):2–9
5. Schroeder AR, Ralston SL. Intravenous antibiotic durations for common bacterial infections in children: when is enough enough? *J Hosp Med*. 2014;9(9):604–609
6. Klein JO, Brunell PA, Cherry JD, Fulginiti VA, eds. *Red Book: 1982 Report of the Committee on Infectious Diseases*. 19th ed. Elk Grove Village, IL: American Academy of Pediatrics; 1982
7. Peter G, Halsey NA, Marcuse EK, Pickering LK, eds. *Red Book: 1994 Report of the Committee on Infectious Diseases*. 23rd ed. Elk Grove Village, IL: American Academy of Pediatrics; 1994
8. Pickering LK, Peter G, Baker CJ, Gerber MA, MacDonald NE, eds. *Red Book: 2000 Report of the Committee on Infectious Diseases*. 25th ed. Elk Grove Village, IL: American Academy of Pediatrics; 2000
9. Rowan JL, Baker CJ. In: Feigin RD, Cherry JD, eds. *Feigen and Cherry's Textbook of Pediatric Infectious Diseases*, 4th ed. Philadelphia, PA: WB Saunders Co; 1998:1089–1106

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10. Broughton DD, Mitchell WG, Grossman M, Hadley WK, Cohen MS. Recurrence of group B streptococcal infection. *J Pediatr*. 1976;89(2):182–185

11. Walker SH, Santos AQ, Quintero BA. Recurrence of group B III streptococcal meningitis. *J Pediatr*. 1976; 89(2):187–188

12. Gras-Le Guen C, Boscher C, Godon N, et al. Therapeutic amoxicillin levels achieved with oral administration in term neonates. *Eur J Clin Pharmacol*. 2007;63(7):657–662

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