Preventing Early Onset GBS Neonatal Sepsis – Are Second Line Intrapartum Antibiotics Equivalent to No Antibiotics at All?

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Strongly encourage pregnant women with the history of a penicillin allergy to undergo prenatal allergy testing as first-line intrapartum antibiotic prophylaxis for group B strep (GBS) is superior to second-line or no antibiotics, which have similar rates of early onset sepsis (EOS). (J Am Board Fam Med 2025;38:1123–1125.)

Keywords: **Drug Allergy, Neonatal Sepsis, Penicillin, Streptococcal Infections**

Strength of Recommendation

B: Patient oriented outcome from a single, high quality cohort study.[1]

Illustrative Case

A 28-year-old female at full term presents to the hospital in active labor. Her group B strep (GBS) status is unknown. The patient states that she had "a bad" reaction to penicillin in her youth, although she does not know exactly what that entailed, and is started on intravenous clindamycin. She has an uneventful delivery 6 hours after antibiotics were initiated, but over the next few hours her baby shows signs of poor feeding and is found to be pale and lethargic. Labs and blood cultures are obtained, and the infant is started on IV ampicillin and gentamycin for presumptive early onset sepsis (EOS). Blood cultures eventually grow GBS. The newborn's clinical status steadily improves, he completes the requisite course of antibiotics, and is discharged from the hospital with his mother who inquires why her baby got GBS infection despite having received intrapartum clindamycin.

Clinical Context

Group B streptococcus is a Gram-positive bacteria that is commonly found in the human genitourinary and gastrointestinal tracts.[2] In most cases, GBS infection in adults is harmless, but in the newborn setting it can pose a serious threat.[2] GBS is currently the leading cause of neonatal infection and the primary risk factor is maternal colonization.[3] Approximately 50% of mothers with GBS colonization will transmit the infection to their neonates via vertical transmission, typically during labor or after rupture of membranes.[3] Without intrapartum antibiotic prophylaxis this leads to approximately 2% of newborns developing early onset GBS infection.[3] With the help of routine screening and intrapartum antibiotics, GBS infection rates in the United States have decreased 80% since 1993 when incidence was 1.7 cases per 1,000 live births compared with 2020 with an incidence 0.2 cases per 1,000 live births.[4] Current practice recommendations from the American College of Obstetrics and Gynecology (ACOG) include universal GBS screening for all pregnant women during the 36th or 37th week of pregnancy.[3] Mothers who screen positive for GBS should receive appropriate intrapartum antibiotic prophylaxis with the exception of a prelabor cesarean birth performed with intact membranes.[3] ACOG guidelines support penicillin being the preferred first-line antibiotic with ampicillin a

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reasonable alternative and cefazolin being used in the setting of a nonanaphylactic penicillin allergy.[3] Acceptable second line antibiotics include clindamycin and vancomycin.[3] Due to increased GBS resistance to clindamycin, sensitivity testing should be obtained with cultures in women with a history of penicillin allergy.[3]

The American Academy of Pediatrics (AAP) recommends intrapartum antibiotic prophylaxis with penicillin, ampicillin or cefazolin as first line antibiotics and clindamycin for those with severe penicillin allergies.

Methods

This article was identified as a potential PURL through the standard systematic methodology that has been described here https://www.jabfm.org/content/37/4/799?ijkey=fe93f26acb7bf7dd96b5dbf3391609a15d3fa892&keytype2=tf_ipsecsha.[5]

An additional literature search was conducted by searching Dynamed, Dynamedex, and UpToDate with the terms "Group B streptococcus," "neonatal sepsis," and "early onset sepsis" to find additional literature to place this research into the context of current clinical practice. A PubMed search of the same terms specifically searching for guidelines from ACOG and AAP also was successfully performed.

Study Summary

This retrospective cohort study was conducted to look at the incidence of GBS EOS among term newborns (define weeks gestation here) whose birth mothers received first line intrapartum antibiotics versus those given second line antibiotics or no antibiotics. The study collected information regarding neonates from a clinical data warehouse connecting electronic medical records from 446 neonatal intensive care units across the United States. The study included term neonates who were discharged from a NICU between 2003 and 2020. Exclusion criteria were neonates with missing information and nonspecific discharge statuses and those with major congenital abnormalities at birth. The primary outcome of concern was the incidence of GBS EOS diagnosed in neonates born at term from GBS positive mothers. First-line therapy was defined as maternal treatment with penicillin, ampicillin, or ampicillin and sulbactam. Antibiotics most commonly used for second-line prophylaxis were cefazolin, clindamycin, and vancomycin. Less commonly used antibiotics for second-line prophylaxis were gentamicin, azithromycin, and oral amoxicillin.

This study's sample size was comprised of 496,180 term neonates, with 104,196 (21%) born to mothers who screened positive for GBS. Within the group of GBS positive mothers, 97,983 had adequate prenatal antibiotic documentation that met the qualifications for the study. Mothers were categorized into 3 groups: first-line (n = 49,234; 50%), second-line (n = 12,679; 13%) and no (n = 36,070; 37%) intrapartum antibiotic treatment.

The overall incidence of GBS EOS was 0.22% (231/104,196). The incidence of GBS EOS in neonates among those who received first-line antibiotics was lower as compared with those who received second-line or no antibiotics (0.1% (51/49,234) vs 0.33% (42/12,679) vs 34% (122/36,070), respectively). Presented in a different way, compared with neonates whose mothers received first-line intrapartum antibiotics, neonates whose mothers received second-line intrapartum antibiotics, or no antibiotics at all had a higher risk for GBS EOS with an adjusted odds ratio (aOR) of 4.1 (95% CI, 2.7-6.4) and 3.8 (95% CI, 2.7-5.4), respectively. A secondary outcome of this study accentuated the fact that there was no significant difference when comparing the rates of GBS EOS in neonates born to mothers who were treated with second line antibiotics versus no antibiotic treatment (aOR, 0.92; 95% CI, 0.64-1.3).[1]

What Is New

Second Line Antibiotics Are Not Effective at Preventing GBS EOS

Patients that are receiving antepartum cefazolin, clindamycin, or vancomycin are at risk of transmitting GBS to the neonate. Incidence of GBS early onset sepsis is equivalent in patients receiving these medications compared with those receiving no antibiotics at all.

Caveats

Does This Mean We Do Not Treat GBS in Penicillin Allergic Patients?

Despite this study demonstrating no significant difference between second-line or no antibiotics, it does not suggest withholding of antibiotic treatment if first line antibiotics are unable to be administered. Rather, these results emphasize how important it is

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to maximize the opportunity to use first-line antibiotics to reduce the risk of GBS EOS. Early penicillin allergy testing (which is safe in pregnancy) should be a routinely pursued to determine those with a type I IgE-mediated hypersensitivity and at a heightened risk of anaphylaxis. For women with the history of a penicillin allergy who have not had allergy testing performed, shared decision making should take place regarding the potential risks and benefits of second-line intrapartum antibiotics.

Challenges to Implementation

Access to Allergy Patch Testing and Clinical Inertia

Not all patients will have easy and affordable access to a dermatology or allergy clinics that perform penicillin patch testing. Fortunately, however, penicillin allergy testing and desensitization is considered safe to do throughout pregnancy, thereby providing time to seek out available options to maximize the potential use of first-line antibiotics for GBS prophylaxis.

In addition, although they also promote expansion of allergy testing as an alternative approach to optimize GBS prophylaxis, ACOG still supports the use of cefazolin, clindamycin, and vancomycin in select patients with a penicillin allergy history who haven't been tested.[3] Indeed, this current study may push clinical guidelines and practice algorithms highlight the importance of penicillin allergy testing and desensitization for the prevention of GBS EOS.

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