EDUCATIONAL COMMENTARY – GROUP B STREP: PREVENTION OF PERINATAL DISEASE

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LEARNING OUTCOMES

On completion of this exercise, the participant should be able to

- describe the clinical syndromes of neonatal group B strep (GBS) infections.
- identify risk factors for early-onset GBS disease.
- summarize the key components of the 2010 CDC GBS prevention recommendations.
- review the laboratory testing methods available for prenatal screening for GBS colonization, noting the advantages and limitations of each.
- recognize the future challenges for the prevention of neonatal GBS disease.

Introduction

Group B Streptococcus (GBS) or Streptococcus agalactiae was recognized as the most common cause of invasive neonatal infections in the 1970s. Initial reports revealed case-fatality rates as high as 50%. The Centers for Disease Control and Prevention (CDC) published official guidelines for the prevention of neonatal GBS infections in 1996, with revisions in 2002 and 2010. Since active prevention measures were instituted, the rate of GBS infections among neonates in the first week of life has declined by 80%. Although the number of neonatal infections has declined substantially over the past 40 years, GBS still remains one of the most common causes of neonatal sepsis in the United States.

Clinical Overview

Neonatal infections with GBS are categorized by two clinical syndromes: early-onset infection, which occurs within the first seven days of life and is characterized by sepsis and pneumonia; and late-onset infection, occurring between day seven and three months of age, characterized by sepsis and meningitis. Early-onset disease accounts for most cases of GBS infection and is caused by vertical transmission of the bacteria from the mother. Colonization of the urogenital or gastrointestinal tract by GBS occurs in 10% to 30% of pregnant women and is the primary risk factor for early-onset disease. Other contributing factors include obstetric complications, prolonged rupture of membranes, and premature birth.

Infants become infected when GBS ascends from the vaginal canal to the amniotic fluid following the onset of labor or rupture of membranes (although this bacterium can invade through intact membranes). The neonate can also acquire GBS during passage through the birth canal. Newborns with early-onset GBS infection usually demonstrate signs of apnea, respiratory distress, or sepsis within the first 24 to 48 hours of life. The mortality rate has declined from 50% in the 1970s to 4% to 6% in more recent years.
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The mortality rate among premature infants, however, is 20% to 30%. The decline of incidence is primarily a result of active prevention measures including screening of pregnant women for the presence of GBS colonization and intrapartum administration of prophylactic antibiotics at least 4 hours before delivery, when indicated.

Late-onset infection appears between one week and three months after birth and often presents as meningitis. This infection is not usually associated with obstetric complications, and GBS screening results are usually negative. The method of transmission for late-onset disease is often not clear. If the mother is positive for GBS then it appears that the infection is due to the passage of the bacteria from mother to baby. If the mother tests negative then it appears that the bacteria is coming from another source. This form of disease is poorly understood. The mortality rate is considerably less than that of early-onset disease. Because the majority of cases are early-onset and effective interventions are available for prevention, the guidelines only concern early-onset disease. The measures used to prevent early-onset GBS disease might also prevent some perinatal maternal infections; however, they do not prevent late-onset infant disease.

2010 CDC Guidelines

The following is a summary of the guidelines provided by the CDC in collaboration with relevant professional societies. Obstetric and neonatal providers in conjunction with supporting laboratories and labor and delivery facilities should adopt the following recommendations for the prevention of early-onset GBS disease:

- Women who have had a previous infant with invasive GBS disease should receive intrapartum antibiotic prophylaxis and do not need third-trimester screening for GBS.
- Women who have GBS isolated from their urine at any time during the current pregnancy should receive intrapartum antibiotic prophylaxis and do not need third-trimester screening for GBS. The presence of GBS bacteriuria at any point during pregnancy is a risk factor for early-onset GBS disease.
- All other pregnant women should be screened for vaginal and rectal GBS colonization between 35 and 37 weeks of pregnancy.
- Antibiotic prophylaxis should be given at the time of labor or rupture of membranes to all pregnant women who test positive for GBS colonization, except for women who deliver by cesarean performed before the onset of labor and in which amniotic membranes are intact. If screening results are not available at the time of labor and delivery, antibiotic prophylaxis should be administered to women who are at less than 37 weeks and 0 days' gestation, have ruptured membranes 18 hours or more before delivery, or have a temperature 100.4°F or higher.
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- Algorithms are available for the management of potential preterm delivery: labor and/or rupture of membranes at less than 37 weeks and 0 days’ gestation.
- Antibiotics should not be administered before the intrapartum period to eradicate GBS genitorectal colonization unless the woman has a GBS urinary tract infection.
- Women should be informed of their GBS screening results and of the recommended interventions.
- For intrapartum antibiotic prophylaxis, penicillin is the agent of choice, and ampicillin is an acceptable alternative. Cefazolin can be used in women who are allergic to penicillin, provided they do not have a history of anaphylaxis, angioedema, respiratory distress, or urticaria following the administration of penicillin or a cephalosporin. Otherwise, clindamycin should be used, provided the GBS isolate is susceptible to clindamycin and erythromycin. In these cases, susceptibility testing must be performed, including testing for inducible clindamycin resistance when applicable. Erythromycin is no longer an acceptable alternative.

Laboratory Testing

The time frame for GBS screening is important, because colonization can be transient and the presence of GBS colonization early in pregnancy is not predictive of early-onset GBS disease. Colonization with GBS late in the third trimester is used as an indicator for intrapartum colonization, thus the recommendation to collect specimens at 35 to 37 weeks. A vaginal and rectal swab (through the anal sphincter) should be collected and placed in an appropriate transport media. A single combined vaginal-rectal swab can be collected. The transport media will maintain the viability of GBS until it arrives in the laboratory. It is recommended that the specimen be stored at room temperature or 4°C until processing. The sensitivity is greatest when the specimen is processed within 24 hours of collection.³

On receipt in the laboratory, the swab should be cultured in selective enrichment broth for 18 to 24 hours at 35° to 37°C. Selective enrichment broths are commercially available, and some contain chromogenic substrates that result in a color change in the presence of β-hemolytic GBS. The advantage of the chromogenic broths is that a positive result may be visible on incubation and no further testing will be necessary. However, non-hemolytic isolates will not be detected by these broths, and subculture will be required. After enrichment, the conventional method for identification of GBS is by subculture of the broth to a blood agar plate and further incubation for 24 to 48 hours at 35° to 37°C. The blood agar plate is then checked for colonies resembling GBS and suspicious colonies are identified using standard techniques. In lieu of the blood agar plate, chromogenic agars are also available that will usually detect isolates by growth of a pigmented colony.
Although culture has been the standard method for GBS screening, it has certain limitations. Culture does not provide rapid results; usually, results take between 24 and 72 hours. In addition, when culture is performed during the recommended third trimester, there are times when the results are not available at the time of labor, or a change in GBS colonization can occur prior to delivery. Finally, women who have no prenatal care or those who deliver preterm do not have access to GBS screening.

In recent years, molecular testing methods have emerged as an alternative approach for the detection of GBS during pregnancy. Molecular methods are available for testing direct vaginal/rectal swabs (non-enriched samples) as well as enriched broth samples. The advantage of molecular techniques is that results can be obtained in a few hours, improving the turnaround time, especially for women in labor with an unknown colonization status. Unfortunately, studies have shown that the sensitivity of nucleic acid amplification tests (NAAT) for GBS detection increases with the use of an enrichment step before testing the sample. Therefore, CDC guidelines indicate that although NAAT can be used, it must be performed after broth enrichment. The enrichment step increases the time to obtain a final result, thus diminishing the advantage of the rapidity of molecular technology. Molecular testing is more costly than culture and requires specialized laboratory equipment and a designated testing area. In addition, with some molecular methods, it is more cost-effective to perform batch testing, which delays the turnaround time. Finally, no isolate is available for antimicrobial susceptibility testing when molecular testing is utilized.

Future Challenges / Summary

There has been remarkable progress in the prevention of perinatal GBS disease, yet significant challenges remain. Although the use of intrapartum antibiotic prophylaxis has reduced the rate of GBS neonatal sepsis, GBS disease still develops in a substantial number of newborns, especially in preterm infants. This most often occurs when women deliver prematurely with an unknown GBS status at delivery because they have not had an opportunity to be tested.

Preterm delivery is not the only problem, however, because GBS develops in some infants who are born to mothers who had negative results at prenatal screening. Since GBS colonization is transient, screening at 35 to 37 weeks may fail to predict the presence of GBS at the time of delivery. Although the current screening strategy is beneficial, there is room for improvement. There is a need for a highly sensitive rapid test to detect GBS in a timeframe that allows patients who require antibiotic prophylaxis to receive appropriate treatment prior to delivery. Ideally, this test should be available around the clock. Finally, the model test should detect resistance markers to guide antibiotic therapy in penicillin-allergic women.
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There is a need for monitoring potential adverse consequences of the increased use of antibiotics. There is concern that the use of intrapartum antibiotic prophylaxis will lead to resistant strains or possibly cause a shift in the profile of causative agents of sepsis from GBS to Gram negative bacteria. Finally, universal screening has had no impact on late-onset GBS disease. More research on preventive measures against late-onset disease is necessary. Perhaps in the future a vaccine will be available to prevent neonatal GBS disease, but until then improved monitoring is imperative.

References and Suggested Reading


