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Group B Streptococcus Intrapartum Prophylaxis Guidelines Adherence: A Perinatal Risk Management Issue

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The intrapartum prevention of group B streptococcus (GBS) bacterial infection in the newborn is based on Centers for Disease Control and Prevention (CDC) guidelines published[1] in 2002 that require universal antepartum screening. An antepartum culture is to be obtained between 35 to 37 weeks' gestation from the vaginal to rectal area; the culture can be safely obtained by the woman herself. Vaginal cultures alone yield only 60% of the GBS identified, compared to those taken from both the vagina and rectum,[2]hence the guidelines require sampling from both areas. The CDC guidelines require intrapartum antibiotic prophylaxis (IAP) to be delivered intravenously by the nursing staff if the woman's culture is positive for GBS or if she has a preexisting risk factor that would indicate the need

for IAP without testing for the presence of GBS colonization. Intrapartum antibiotic prophylaxis was based on 5 controlled trials that support efficacy of the approach in reducing neonatal GBS infection.[3]

The guidelines were specifically intended to reduce the rate of early onset group B streptococcus (EOGBS) disease, which is associated with significant newborn mortality and morbidity with profound sequelae. Early onset group B streptococcus infections occur in the first week of life; prevention has presented a major challenge in perinatal nursing practice. When neonatal EOGBS disease occurs, it has a 5% to 10% mortality rate.[4] The implementation of the 2002 CDC guidelines[1] has reduced the overall incidence of invasive neonatal EOGBS infection. For example, in one study[5] that included 5 states, the rates of EOGBS declined from 0.47 cases per 1000 live births in 1999–2001 to 0.34 cases from 2003–2005, which amounts to a 27% reduction. Compared to a decade earlier, when the rate in 1993 was reported to be 1.7 cases per 1000 live births, the decreased incidence of EOGBS disease is even more evident. To further reduce EOGBS disease, adherence to the GBS guidelines based on antepartum test results, with IAP given to appropriate candidates, has important risk management considerations. It was estimated that timely administration of IAP could prevent as much as 80% of perinatal GBS infections.[6] A portion of the EOGBS residual infections may be related to the approximately 4% of women with false-negative cultures during the third trimester.[7]Another smaller portion of the EOGBS infections could be due to nonadherence to the GBS guidelines.[8]

SOURCE OF GBS

Early onset group B streptococcus infections are almost exclusively the result of vertical transmission from the mother.[9] Fully, 80% of all the neonatal GBS infections[1] are early onset and associated with a significant portion of the GBS-related mortality.[4] (Late onset GBS disease, defined as occurring from 1 week up to 3 months (89 days) after birth, is differentiated as a separate entity, is not addressed in the CDC guidelines,[1] and is beyond the scope of this article.)

Independent of hygiene, most vaginal bacteria originate and ascend from intestinal microbes.[10] Group B streptococcus is normal flora present in the gastrointestinal track and vaginas of 10% to 30% of women. Variation is noted by ethnicity, with African American women having higher rates of GBS-positive cultures (up to 40.6%) and heavier colonization than women of other ethnic groups.[11] Heavier colonization is directly related to the risk of giving birth to a GBS-colonized infant.[11] Group B streptococcus colonization may be transient, intermittent, or chronic.[1,12] In healthy pregnant women, this normal flora may be vertically transmitted to infants during birth and lead to EOGBS infections even if the amniotic membranes are intact.[13] Of colonized women, it is estimated that the rate of maternal-neonatal transmission is 1% to 2%, with 3% to 12% of neonates developing bacteremia resulting in EOGBS disease.[4]

INTRAPARTUM ANTIBIOTIC PROPHYLAXIS

On the basis of the population incidence of colonization, the universal testing approach potentially results in IAP exposure for 10% to 40% of laboring women. Penicillin (PCN) G is the preferred antibiotic for IAP; ampicillin can be used to replace PCN, but not if the woman has a PCN allergy. Alternative antibiotic selection is based on a history of allergies and GBS susceptibility to various antibiotic agents. The other medications that can be substituted in particular situations are erythromycin, clindamycin, cefazolin, or vancomycin. For women with PCN allergies who are at low risk of anaphylaxis, cefazolin is

the recommended IAP agent.[6] If the PCN-allergic woman's culture results indicate resistance or susceptibility is unknown, vancomycin is indicated.[6]

Antibiotic resistance is a growing concern especially for PCN-allergic women.[6] Thus far, a less than 2% resistance to PCN has been reported.[14] However, 2 of the substitutes for PCN-allergic women, erythromycin and clindamycin, are increasingly associated with GBS resistance.[6,15] Therefore, routine testing for antibiotic susceptibility is recommended when women are not PCN candidates.[16,17] Regardless of the chosen medication for IAP, nursing responsibilities include monitoring for allergic reactions to the agent administered.

According to the 2002 CDC guidelines,[1] optimal prophylaxis is 4 hours prior to birth.[6] If labor continues beyond that point, the guidelines direct that IAP be repeated every 4 hours. Several studies have shown that the 4-hour time frame was not scientifically determined. Colombo and colleagues[18] examined 21 women with scheduled cesarean sections who received intravenous ampicillin before delivery and agreed to simultaneous blood sampling when the newborn cord blood was drawn at birth. The shortest IAP to birth time was 27 minutes; by that time, the bactericidal level in the cord blood was adequate. The bactericidal levels continued to increase in a linear relationship up to 5.6 hours following dosing, which was the longest interval to delivery in the study.[18] Illuzzi and Bracken[19] conducted a systematic review of 4 studies and found that the incidence of GBS-colonized neonates born to GBS-positive mothers decreased substantially within 1 to 2 hours of IAP. The authors added that the pharmacokinetic data did not support the rationale for the 4-hour time frame. Bloom and associates[20] documented that bactericidal concentrations of ampicillin in fetal and maternal blood were reached within 3 minutes and in amniotic fluid within 5 minutes during elective cesarean sections. Thus, invasive newborn testing and separation from mothers for extended observations may not be indicated when IAP was administered less than 4 hours prior to birth.

CONTINUED CHALLENGES

While IAP for women colonized with GBS has successfully reduced the incidence of EOGBS, it is not without consequences. The 2002 CDC guidelines[1] include treatment of GBS-positive women with IAP; however, the problem of neonatal EOGBS infections has not been eradicated.

Mortality is significantly higher in preterm infants, with prematurity accounting for two thirds of all GBS-related deaths.[4] Therefore, a woman who is in active preterm labor with an unknown GBS status, and expected to deliver preterm, should receive IAP. Given that women with a late preterm infant do not commonly receive tocolytic agents and the course of labor may be rapid, there is a risk that GBS prevention may not occur.

Group B streptococcus can be identified on routine urine cultures done any time during pregnancy. The incidence of antenatal GBS bacteriuria is estimated[9] at 2% to 4%. Prompt treatment of the urinary tract infection following diagnosis is necessary. Group B streptococcus cultures during the third trimester are not indicated for women affected with GBS bacteriuria; they are considered heavier colonizers of GBS and require IAP because their infants are at greater risk of EOGBS infections.[1] The same holds true for a woman who has given birth previously to an infant with an invasive GBS infection. These mothers are also considered heavier colonizers and therefore at high risk of transmitting GBS to subsequent neonates; they are to receive IAP without the need for antepartal culturing.[1]

The intrapartum care of a woman with unknown GBS status presents an additional challenge for nurses and other healthcare providers. When the GBS status is unknown, the woman should be treated using a risk-based approach.[1] When a culture was not obtained prenatally or the result is unknown, women who have one of the following risk factors should receive IAP: (1) less than 37 weeks' gestation with anticipation of delivery, (2) rupture of membranes greater than or equal to 18 hours, and (3) maternal temperature greater than or equal to 100.4°F. Women who have unknown GBS status without any risk factors should not receive IAP. Conversely, IAP is not indicated when women have a negative GBS culture in the third trimester, even if an intrapartum risk factor develops.[1]

ONGOING NEONATAL CONCERNS

The symptoms of EOGBS include respiratory instability, apnea, lethargy, and hypotension.[21] These symptoms manifest quickly. For example, a study of 277 912 live births identified 172 infants with positive GBS cultures and clinical signs of EOGBS infection. Of these, 95% were symptomatic within 24 hours, another 3.7% within 48 hours, with only 1.2% demonstrating symptoms after 48 hours.[22] Therefore, the vast majority of EOGBS infections will be detectible within one day of life.[22] In affected neonates, bacteremia, meningitis, and pneumonia may result. Approximately, 5% of neonatal bacteremia is thought to be nosocomial in origin,[4] highlighting the nursing responsibility of careful hand washing during client care.

While IAP is protective, it is not without neonatal consequences. Ampicillin is a broad spectrum antibiotic, and therefore is more likely to lead to problems with antibiotic resistance. Although data are based on a small number of cases, the incidence of *Escherichia coli* bacteremia appears to have increased, especially in very low-birth-weight neonates.[4] This may be attributable to ampicillin resistant *E coli* strains, but evidence linking it specifically to IAP is lacking.[4] Intrauterine exposure to broad spectrum antibiotics may alter the neonatal gut flora in ways that might have long-term effects and could be related to the development of allergic sensitivity.[23]

CLINICAL IMPLICATIONS

Pinto and colleagues[24] speculated about multiple causes of residual cases of EOGBS infections despite the use of the CDC guidelines.[1] These included confusion about existing guidelines, lack of access to GBS culture results on admission, rapid labor progress, and maternal refusal of IAP. Knowledgeable perinatal nurses can impact the first two issues and use careful documentation to explain the lack of IAP for the latter two.

Several strategies can improve adherence to the CDC guidelines[1] and therefore reduce residual cases of EOGBS. For example, preprinted orders can streamline the initiation of IAP. The intrapartum nurse needs to locate the culture result and also confirm when the specimen was collected. Group B streptococcus culture results taken 6 weeks or more prior to birth have only a 43% sensitivity and a 85% specificity. This is contrasted with cultures taken between 1 to 5 weeks prior to delivery that have a 87% sensitivity and a 96% specificity.[7]

Adherence to the 2002 CDC guidelines[1] has resulted in a significant decrease in EOGBS infections. One concern for women and nurses is the timing of IAP. Penicillin and ampicillin are the only recommended antibiotics that require redosing every 4 hours until birth. On the basis of the studies of ampicillin

administration that identified that bacteriocidal levels were rapidly achieved in both the mother and fetus following IAP, a woman can be reassured that she is likely adequately prophylaxed prior to the 4-hour time frame suggested in the guidelines.[18] Further, if there is a delay in administering a repeat IAP dose, Colombo and colleagues[18] documented bactericidal concentrations up to 5.6 hours post-IAP. The antibiotics appropriate for PCN-allergic women are given every 6 to 12 hours, depending on the agent used.[1] This knowledge can be shared with women. Because women can become ill with chorioamnionitis, endometritis, postpartum wound infections, and septicemia as a result of GBS,[25] IAP also may avert serious maternal infections.

FUTURE DIRECTIONS

Nurses need to remain current as guidelines and diagnostics change. For example, a rapid GBS test done during intrapartum care may improve detection of GBS colonization at the time of birth.[8] A maternal GBS vaccine is in development but far from use in the general population.[26] While it is true that in the future GBS management may change, lack of adherence to the current prevention guidelines is not optional.

Creative approaches are needed to further eliminate the incidence, and the profound consequences, of residual cases of neonatal EOGBS disease. Despite the successes attributable to the current guidelines, the amount of treatment required and the related costs cannot be ignored. Furthermore, the long-term consequences of IAP, including repeated dosing, for women and infants have not been documented. The use of IAP alters normal birth for almost one third of all women. Just the necessity of an intravenous catheter can create an atmosphere that medicalizes the experience. In addition, parents worry about GBS throughout late pregnancy and birth, particularly in terms of the timing of their entry into the birth environment to receive IAP. The parents' emotional issues associated with GBS colonization warrant investigation. Facilitating IAP in an out-of-hospital birth setting adds technologic complexity. For example, home birth practitioners must transport the necessary equipment and supplies. The cumulative impact of GBS colonization on normal birth processes needs investigation. These authors plan to explore the impact of probiotics on GBS colonization in pregnant women. It is hoped that the prenatal use of probiotics will alter the maternal gut and vaginal flora to reduce the incidence of GBS colonization in late pregnancy.

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REFERENCES

1. Center for Disease Control and Prevention. Prevention of perinatal group B streptococcal disease. Revised guidelines from CDC. *MMWR Morb Mortal Wkly Rep*. 2002;51(RR-11):1–22.
2. Philipson EH, Palermino DA, Robinson A. Enhanced antenatal detection of group B streptoccoccus colonization. *Obstet Gynecol.* 1995;85:437–439.
3. Smaill FM. Intrapartum antibiotics for group B streptococcal colonisation. *Cochrane Database Syst Rev.* 2000;(2):CD000115. doi: 10.1002/14651858.CD000115.

4. Gilbert R. Prenatal screening for group B streptococcal infection: gaps in the evidence. *Int J Epidemiol*. 2003;33(1):2–8.
5. Phares CR, Lynfield R, Farley MM, et al. Epidemiology of invasive group B streptococcal disease in the United States, 1999–2005. *JAMA*. 2008;299:2056–2065.
6. Apgar BS, Greenberg G, Yen G. Prevention of group B streptococcal disease in the newborn. *Am Fam Phys*. 2005;71(5):903–910.
7. Yancey MK, Schuchat A, Brown LK, Ventura VL, Markenson GR. The accuracy of late antenatal screening cultures in predicting genital group B streptococcal colonization at delivery. *Obstet Gynecol*. 1996;88(5):811–815.
8. Puopolo KM, Madoff LC, Eichenwald EC. Early-onset group B streptococcal disease in the era of maternal screening. *Pediatrics.* 2005;115(5):1240–1246.
9. Persson K, Christensen KK, Christensen P, Forsgren A, Jorgensen C, Persson PH. Asymptomatic bacteriuria during pregnancy with special reference to group B streptococci. *Scand J Infect Dis.* 1985;17:195–199.
10. Bolton M, Van Der Straten A, Cohen CR. Probiotics: potential to prevent HIV and sexually transmitted infections in women. *Sex Transm Infect*. 2008;35(3):214–225.
11. Hickmann ME, Rench MA, Ferrieri P, Baker CJ. Changing epidemiology of group B streptococcal colonization. *Pediatrics.* 1999;104:203–209.
12. Dillon HC, Gray E, Pass MA, Gray BM. Anorectal and vaginal carriage of group B streptococci during pregnancy. *J Infect Dis*. 1982;145(6):794–799.
13. Turow J, Spitzer AR. Group B streptococcal infection early onset disease controversies in prevention guidelines, and management strategies for the neonate. *Clin Pediatr.* 2000;39:317–326.
14. Bland ML, Vermillion ST, Soper DE, Austin M. Antibiotic resistance patterns of group B streptococci in late third-trimester rectovaginal cultures. *Am J Obstet Gynecol*. 2001;184:1125–1126.
15. Heelan JS, Hasenbein ME, McAdam AJ. Resistance of group B streptococcus to selected antibiotics, including erythromycin and clindamycin. *J Clin Microbiol.* 2004;42(3):1263–1264.
16. Pearlman MD, Pierson CL, Faix RG. Frequent resistance of clinical group B streptococci isolates to clindamycin and erythromycin. *Obstet Gynecol*. 1998;92:258–261.
17. Chohan L, Hollier LM, Bishop K, Kilpatrick CC. Patterns of antibiotic resistance among group B streptococcus isolates: 2001–2004. *Infect Dis Obstet Gynecol*. 2006;2006:57492.
18. Colombo DF, Lew JL, Pedersen CA, Johnson JR, Fan-Havard P. Optimal timing of ampicillin administration to pregnant women for establishing bactericidal levels in the prophylaxis of Group B Streptococcus. *Am J Obstet Gynecol*. 2006;194:466–470.
19. Illuzzi JL, Bracken MB. Duration of intrapartum prophylaxis for neonatal group B streptococcal disease: a systematic review. *Obstet Gynecol*. 2006;108(5):1254–1265.
20. Bloom SL, Cox SM, Bawdon RE, Gilstrap LC. Ampicillin for neonatal group B streptococcal prophylaxis: how rapidly can bactericidal concentrations be achieved? *Am J Obstet Gynecol*. 1996;175:974–976.
21. Cunningham FG, Leveno KJ, Bloom SL, Hauth JC, Rouse DJ, Spong CY. Infectious diseases: bacterial infections. In: *Williams Obstetrics*. 23rd ed. New York, NY: McGraw Hill; 2010:1220–1223.
22. Bromberger P, Lawrence JM, Braun D, Saunders B, Contreras R, Petitti DB. The influence of intrapartum antibiotics on the clinical spectrum of early-onset group B streptococcus infection in term infants. *Pediatrics.* 2000;106(2):244–250.

23. Bedford Russell AR, Murch SH. Could peripartum antibiotics have delayed health consequences for the infant? *BJOG.* 2006;113:758–765.
24. Pinto NM, Soskolne EI, Pearlman MD, Faix RG. Neonatal early-onset group B streptococcal disease in the era of intrapartum chemoprophylaxis: residual problems. *J Perinatol.*2003;23:265–271.
25. Picard FJ, Bergeron MG. Laboratory detection of group B Streptococcus for prevention of perinatal disease. *Eur J Clin Microbiol Infect Dis*. 2004;23:665–671.
26. Larsen JW, Sever JL. Group B Streptococcus and pregnancy: a review. *Am J Obstet Gynecol.* 2008;198(4):440–450.