Duration of antimicrobial prophylaxis for group B streptococcus in patients with preterm premature rupture of membranes who are not in labor

Jesus R. Alvarez, MD; Shauna F. Williams, MD; Vijaya L. Ganesh, MD; Joseph J. Apuzzio, MD

OBJECTIVE: The purpose of this study was to determine the duration of the time that is needed to eradicate group B Streptococcus (GBS) in pregnant women with preterm premature rupture of membranes (PPROM).

STUDY DESIGN: A retrospective cohort study was performed of pregnant women with PPROM from January 1, 2000, through December 31, 2005. Vaginal/rectal cultures were performed on admission and repeated daily. Patients received antibiotics until cultures were negative for 3 consecutive days.

RESULTS: Two hundred fourteen women were identified with PPROM; 169 of the women met the inclusion criteria. Thirty-three patients were GBS positive on admission and had negative cultures by day 3. Neonatal sepsis occurred in 19 neonates (11.2%); 3 neonates (16%) were from mothers who tested positive for GBS on admission, and 16 neonates (84%) were from mothers who tested negative on admission. There were no cases of neonatal sepsis because of GBS.

CONCLUSION: A 3-day regimen of antibiotic prophylaxis appears to be adequate to eradicate GBS from the genital tract of patients with PPROM.

Key words: group B streptococcus, neonatal sepsis, PPROM

Cite this article as: Alvarez JR, Williams SF, Ganesh VL, Apuzzio JJ. Duration of antimicrobial prophylaxis for group B streptococcus in patients with preterm premature rupture of membranes who are not in labor. Am J Obstet Gynecol 2007;197:390.e1-390.e4.

Group B streptococcus (GBS) remains a leading cause of serious neonatal infection, despite great progress in perinatal GBS disease prevention.[1] It colonizes approximately 10%-30% of all pregnant women.[2,3] GBS may be transmitted vertically to the newborn infant by either ascending infection after rupture of the fetal membranes or by acquisition during vaginal delivery. GBS may cause both an early-onset neonatal disease within the first 5 days of life and a late-onset disease, which occurs after the first week of life. The incidence of early-onset GBS disease among neonates who are born to colonized mothers is approximately 0.5%.[4] Late-onset GBS disease is not believed to be associated with obstetric factors.

The neonatal mortality rate from GBS infections was reported to be as high as 50% before 1980 and has decreased to 4% as the result of intrapartum chemoprophylaxis and advances in neonatal care.[5,6] The American College of Obstetricians and Gynecologists and the Centers for Disease Control and Prevention (CDC) developed recommendations in 1996 for intrapartum chemoprophylaxis to prevent perinatal GBS disease.[7,8] The CDC later updated these guidelines in 2002.

Preterm premature rupture of membranes (PPROM) refers to rupture of membranes (ROM) before 37 weeks of gestation and accounts for close to one-fourth of all cases of ROM. PPROM accounts for nearly 40% of all preterm births.[9] Multiple studies in the 1980s reported an increased association between PPROM, low birthweight neonates, and early-onset GBS neonatal disease.[3,10,11] A multicenter case-control study by Schuchat et al[12] reported that a risk-based strategy for chemoprophylaxis potentially could prevent a substantial portion of GBS cases. One of the risk factors identified by Schuchat et al that increased the incidence of early-onset GBS disease was ROM of >18 hours.

The CDC algorithm for GBS prophylaxis for women with threatened preterm delivery that included those with PPROM includes prescribing intravenous penicillin for at least a total of 48 hours; at the physician's discretion, the antibiotic prophylaxis may be continued beyond 48 hours.[1]

Our hypothesis is that GBS can be cleared from the genital tract with <3 days of antimicrobial therapy. Daily cultures for GBS were obtained from the lower genital tract of patients with PPROM. We reviewed the culture results to determine the duration of time that antimicrobials were needed to eradicate GBS from the lower genital tract of women with PPROM.

Materials and Methods

A retrospective cohort study was performed for all women who were admitted with PPROM to University Hospital, Newark, NJ, from Jan. 1, 2000, through Dec. 31, 2005. The study was approved by the institutional review board of UMDNJ–New Jersey Medical School.

From the Department of Obstetrics, Gynecology and Women's Health, UMDNJ–New Jersey Medical School, Newark, NJ.

Presented at the 27th Annual Clinical Meeting of the Society for Maternal-Fetal Medicine, San Francisco, CA, Feb. 5-10, 2007.

Received Mar. 10, 2007; revised May 17, 2007; accepted June 25, 2007.

Reprints: Joseph J. Apuzzio, MD, UMDNJ-New Jersey Medical School, 185 South Orange Ave, MSB E565, Newark, NJ 07101-1709; joseph.apuzzio@umdnj.edu.

0002-9378/$32.00

doi: 10.1016/j.ajog.2007.06.047

TABLE
Demographic characteristics

Characteristic	GBS positive (n = 33)	GBS negative (n = 136)	*P* value
Age (y)*	28 (16-40)	29 (15-42)	≤.993†
Gestational age on admission (wk)*	29 (25-34)	30 (24-34)	≤.563†
Gestational age at delivery (wk)*	30 (25-34)	31 (22-34)	≤.257†
Latency period (d)*	6 (3-17)	4 (3-33)	≤.653†
No prenatal care (d)	14 (42.4%)	27 (19.8%)	≤.05‡
Cesarean delivery rate (n)	17 (51.5%)	74 (54.4%)	≤1.0‡

* Data are given as median (range).

† Mann-Whitney *U* test.

‡ Chi-square test.

Patients with a complaint of leakage of fluid per vagina were evaluated in the labor and delivery triage area by a sterile speculum examination. ROM was confirmed with visualization of fluid from the cervical os, a positive fern, and nitrazine test. Patients with confirmed PPROM at ≥34 weeks of gestation were delivered. Patients with PPROM that was confirmed at a gestational age of <34 weeks of gestation and without signs of fetal distress, infection, or labor were admitted to the antepartum service for expectant treatment and complete bed rest. One specimen for culture for GBS was obtained on admission and daily thereafter from both the lower one-third of the vagina and rectum. The specimens were processed in selective media as per CDC recommendations. Patients were prescribed intravenous antibiotics until the GBS cultures were negative for 3 consecutive days. Patients were excluded if GBS cultures were not performed on the day of admission (day 0) or if they delivered within 48 hours of admission.

All such patients who were admitted to the antepartum service received a course of antenatal corticosteroids, either betamethasone or dexamethasone, if betamethasone was not available. A *course of corticosteroids* was defined as either betamethasone 12.5 mg intramuscularly every 24 hours for 2 doses or dexamethasone 6 mg intramuscularly every 12 hours for 4 doses.

Penicillin G was the primary antibiotic used for GBS prophylaxis in PPROM. The dose of penicillin was 5 million units of intravenous penicillin G as a loading dose, followed by 2.5 million units every 4 hours until the GBS cultures were negative for 3 consecutive days as per departmental protocol. The admission GBS culture that was obtained from patients who were allergic to penicillin was tested for resistance to clindamycin. Penicillin-allergic patients received 900 mg of intravenous clindamycin as a loading dose, followed by 900 mg intravenously every 8 hours. The antibiotic was changed according to the sensitivity, if necessary. Based on the 2002 CDC guidelines, penicillin-allergic patients with PPROM received 1 g of vancomycin intravenously every 12 hours for GBS prophylaxis. No other antimicrobials were prescribed.

Patients who were admitted had orders for complete bed rest and daily monitoring with nonstress test and twice weekly biophysical profiles. Patients were monitored for any signs of infection with a complete blood count with differential twice a week and the white blood cell count was monitored. Patients were delivered if there was a nonreassuring fetal heart tracing or rising leukocytosis or if intraamniotic infection occurred. Intraamniotic infection was diagnosed by the presence of uterine tenderness, leukocytosis, and temperature >100.4°F without another source of infection. Every patient received intrapartum antimicrobials, except in the setting of a patient having 3 consecutive negative GBS cultures and without a suspicion of intraamniotic infection.

We reviewed the incidence of neonatal sepsis in our PPROM population. Bacterial identification and sensitivity were obtained for the culture-positive neonates. Neonatal blood cultures were done on admission to the neonatal intensive care unit as per departmental protocol, and neonatal sepsis was considered if these were positive. The presence of GBS colonization in mothers was assessed for neonates who were diagnosed with sepsis. Placenta were sent to the pathology department for a histologic examination after delivery, as ordered by the attending physician. We also compared intraamniotic infection with histologic chorioamnionitis of the placenta.

Results

A total of 214 patients were identified as having PPROM at <34 weeks of gestation. We excluded 45 patients from the study group because 23 women were in active labor and 22 other patients did not have GBS cultures done on admission (day 0). A total of 169 patients met the inclusion criteria of having GBS cultures on admission who were admitted for expectant treatment to the antepartum service. Of the 169 patients, 33 women (19.5%) were GBS positive, and 136 women (80.5%) were GBS negative on admission (Table). There were 6 multifetal pregnancies; therefore, a total of 140 neonates were born from the GBS negative group and 35 neonates were born to the GBS-positive group.

In the GBS-positive carrier group, the daily genital tract cultures for GBS were negative in 29 patients (88%) by day 1, in 32 patients (97%) by day 2, and in all 33 patients (100%) by day 3. The median latency period until delivery for this group was 6 days (range, 3-17; Table 1). Of the 33 patients in this group, 31 women received chemoprophylaxis with penicillin G, and 2 women received clindamycin.

From the group of PPROM mothers with negative GBS cultures on admission, 2 of 187 patients reverted to being positive on day 1. They both had 3 consecutive genital cultures after day 1. No cultures in the GBS-negative group re-