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No increase in rates of early-onset neonatal sepsis by antibiotic-resistant group B *Streptococcus* in the era of intrapartum antibiotic prophylaxis

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Objective: The aim of this study was to assess the rate of early-onset neonatal sepsis by antibiotic-resistant group B *Streptococcus*.

Study design: The time-trend study was conducted at a tertiary care center over the following periods: no protocol for group B *Streptococcus* prophylaxis (1990 to 1992), risk-based protocol (1993 to 1996), and screening-based protocol (1997 to 2002).

Results: A total of 120,952 neonates were born with 118 cases of group B *Streptococcus* early-onset neonatal sepsis. The rate of group B *Streptococcus* early-onset neonatal sepsis decreased significantly (from 2.0 to 1.1 to 0.4 per 1000 births, $P < .0001$). No group B *Streptococcus* isolate was resistant to ampicillin, penicillin, cefazolin, or vancomycin. From 1997 to 2002, there were 3 clindamycin-resistant group B *Streptococcus* isolates (14%). The rate of erythromycin-resistant group B *Streptococcus* early-onset neonatal sepsis did not change (from 0.14 to 0.03 to 0.08 per 1000 births, $P = .6$). However, cases of erythromycin-resistant group B *Streptococcus* early-onset neonatal sepsis accounted for an increasing proportion of the remaining cases of group B *Streptococcus* early-onset neonatal sepsis (from 7.0% to 2.6% to 23.8%, $P = .07$).

Conclusion: We found no increase in rates of antibiotic-resistant group B *Streptococcus* early-onset neonatal sepsis.

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Intrapartum antibiotic prophylaxis (IAP) is the most effective strategy to prevent neonatal group B *Streptococcus* (GBS) disease. In 1996 the Centers for Disease Control and Prevention (CDC) published consensus guidelines in the United States that endorsed either a risk-based or a screening-based protocol for administering IAP.[1] The recommended antibiotics for prophylaxis were penicillin G and in penicillin-allergic mothers, erythromycin or clindamycin. A multistate time-trend study has subsequently shown a substantial decrease in the rate of early-onset neonatal sepsis (EONS) caused by GBS by the late 1990s.[2] In 2002, the CDC revised its guidelines to recommend a universal screening-based strategy and a complicated algorithm for penicillin-allergic mothers, which included prophylaxis with 1 of 4 antibiotics (cefazolin, erythromycin, clindamycin, and vancomycin), depending on clinical and microbiologic information.[3]

The CDC has estimated that with implementation of a screening-based protocol, more than a quarter of women will be exposed to antibiotics during the intrapartum period.[1] This widespread use of intrapartum antibiotics has led to concern about the potential for an increase in the development of EONS caused by antibiotic-resistant organisms.[3,4] Time-trend studies have been conducted to evaluate the changes in rates of EONS caused by antibiotic-resistant organisms. Our previous work[5] did not show a change in the rates of EONS caused by ampicillin-resistant organisms in the mid-1990s. Other studies that analyzed the proportion, and *not* rates, of EONS caused specifically by ampicillin-resistant *Escherichia coli* in the late 1990s showed inconsistent results, with some finding an increase[6,7] and others an initial increase and then a decrease.[8] However, these findings are difficult to interpret because changes in the proportion of EONS cases caused by ampicillin-resistant *E. coli* could result from either an increase in EONS cases because of resistant organisms or a decrease in EONS cases because of susceptible organisms.

Changes in the rates of EONS caused by GBS resistant to antibiotics other than ampicillin have not been evaluated fully. Some GBS isolates from pregnant women are known to exhibit resistance to erythromycin or clindamycin or both.[9-11] One time-trend study showed an increase in the proportion of GBS-colonizing isolates from pregnant women who were erythromycin-resistant.[12] Studies in neonates of invasive GBS isolates have shown that some infections were caused by organisms resistant to erythromycin or clindamycin or both.[13,14] Whether there has been a change in the rate of EONS by such antibiotic-resistant GBS in the era of IAP is not known.

We conducted this time-trend study to assess the rates of EONS by antibiotic-resistant GBS in a large maternity service over a 13-year study period that encompassed a hospital's sequential implementation of risk-based and screening-based protocols for IAP for the prevention of neonatal GBS disease.

Methods

We performed a time-trend study of the rates of EONS among infants born at the Brigham and Women's Hospital, a tertiary care referral center, over a 13-year period from January 1, 1990, through December 31, 2002. The study was approved by the hospital institutional review board. From 1990 to 1992, there was no protocol for GBS prophylaxis. By 1993, a risk-based protocol was in place; IAP was given to women in labor who had risk factors for GBS transmission (eg, preterm delivery, intrapartum fever, prolonged rupture of membranes). By 1997, the risk-based protocol was changed to a screening-based protocol. Under this protocol IAP was given to women in labor who screened positive for GBS colonization by vaginal and rectal screening culture obtained at 35 to 37 weeks' gestation. In the risk-based protocol, ampicillin was used for intrapartum prophylaxis (clindamycin in penicillin-allergic mothers). In the screening-based protocol, penicillin G was recommended for intrapartum prophylaxis (erythromycin or clindamycin in penicillin-allergic mothers).

Data on cases of GBS EONS and antibiotic susceptibility were obtained from the hospital microbiology database. A neonate was considered to have GBS EONS if GBS was isolated from a blood culture within the first 7 days of life. The isolate's susceptibility to ampicillin, penicillin, erythromycin, clindamycin, cefazolin, and vancomycin was recorded. The microbiology laboratory personnel used disc diffusion methods to determine antibiotic susceptibility. The zone sizes were graded as sensitive, intermediate, and resistant. Break points used for distinguishing susceptibility to erythromycin were 15 millimeters or less, resistant; 16 to 20 mm, intermediate; and 21or more, sensitive. Break points used for distinguishing susceptibility to clindamycin were 15 mm or less, resistant; 16 to 18 mm, intermediate; and 19 mm or more, sensitive.

To analyze changes in rates and proportions of EONS over time, we used the χ^2 test for linear trend (Epi Info 6.04b Centers for Disease Control and Prevention, Atlanta, Ga).

Results

The number of neonates born in each time period and the number of neonates with GBS EONS are listed in Table I. There was a significant decrease in rate of GBS EONS across the 3 time periods (from 2.0/1000 births with no protocol for GBS prophylaxis to 1.1/1000 births with a risk-based protocol to 0.4/1000 births with a screening-based protocol, $P < .0001$, Table II). Over