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Clindamycin-Resistant Group B *Streptococcus* and Failure of Intrapartum Prophylaxis to Prevent Early-Onset Disease

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Abstract

Guidelines recommend intrapartum antibiotic prophylaxis (IAP) for parturient women who have a screen positive for group B *Streptococcus* (GBS). Clindamycin should be used for IAP only if the maternal GBS isolate is susceptible. We report a case of clindamycin-resistant GBS disease in a newborn infant whose mother received clindamycin IAP, and we review clindamycin susceptibility testing.

During the 1970s, group B *Streptococcus* (GBS) disease emerged as the leading cause of neonatal morbidity and mortality in the United States.^{1,2} The Centers for Disease Control and Prevention (CDC) 2002 guidelines recommend routine screening of all pregnant women for recto-vaginal GBS colonization at 35 to 37 weeks' gestation and the administration of intrapartum antibiotic prophylaxis (IAP) during labor for those whose screen is positive.³ Implementation of universal screening for GBS and IAP administration has reduced the incidence of early onset GBS disease (infection occurring before 7 days of age) from 1.8 cases per 1000 live births in 1990 to 0.34 cases per 1000 live births by 2007.^{4,5}

GBS remains universally susceptible to penicillin,⁶ and penicillin is the preferred agent for IAP. However, women with penicillin allergy require alternatives. The CDC guidelines recommend that patients with documented penicillin allergy who are not at high risk for anaphylaxis receive cefazolin.⁷ For penicillin-allergic women at high risk for anaphylaxis, GBS isolates should be tested for susceptibility to clindamycin and erythromycin.⁹ Clindamycin should be used for IAP only if the GBS isolate is susceptible to both antibiotics, as in vitro erythromycin resistance often predicts in vivo clindamycin resistance. Vancomycin is recommended for IAP only in penicillin-allergic women at high risk for anaphylaxis because efficacy in preventing GBS disease has not been demonstrated and pharmacokinetics is not ideal.³

Recent studies demonstrate that the proportion of GBS isolates with in vitro clindamycin and erythromycin resistance is rising.^{6,8,9} The CDC guidelines for the prevention of

perinatal GBS disease were specifically updated in 2002 to provide guidance for susceptibility testing.³ Despite these recommendations, susceptibility testing is not consistently performed.¹⁰ Few documented cases of clindamycin-resistant early-onset GBS disease after maternal IAP with clindamycin have been reported.¹¹ Here we describe a case of clindamycin-resistant early-onset GBS disease in which the mother received clindamycin IAP without susceptibility testing. We review the literature describing clindamycin resistance and adherence to susceptibility testing guidelines and perform an analysis of GBS resistance rates, susceptibility testing, and IAP in our own health care system.

Case Report and Hospital Data

A Caucasian male was born via spontaneous vaginal delivery at 39 weeks' gestation. The infant's mother had recto-vaginal cultures positive for GBS at 34 and 35 weeks. Although the mother was known to have a penicillin allergy, the nature of this allergy was not documented, and susceptibility studies were not performed on either isolate.

The mother presented in active labor, and clindamycin was administered as IAP 4 hours before delivery. Membranes were ruptured artificially 30 minutes before delivery. Apgar scores were 8 and 8 at 1 and 5 minutes, respectively.

The newborn infant had respiratory distress within the first hour of life. A blood culture was obtained, and treatment was initiated with ampicillin and gentamicin. Chest radiography demonstrated bilateral granular infiltrates. The infant required mechanical ventilation and inotropic pressor support. The blood culture was positive for GBS, susceptible to penicillin and vancomycin, but resistant to clindamycin (minimum inhibitory concentration $>2 \mu\text{g}/\text{mL}$). A repeat blood culture obtained 32 hours after delivery remained positive. A third blood culture at 72 hours was negative. Cerebrospinal fluid obtained 96 hours after delivery showed no pleocytosis, and culture was negative. Intravenous ampicillin and gentamicin were continued for a total of 12 days. The infant was discharged home on day 13.

Intermountain Healthcare is a nonprofit integrated delivery system operating 22 hospitals with ~30 000 births per year. A review of microbiology data from October 1, 2007, to September 30, 2008, demonstrated rates of clindamycin and erythromycin resistance among GBS isolated from maternal screens of 24% and 44%, respectively. Over this period, there were 3698 maternal screens positive for GBS; however only 138 isolates (4%) underwent susceptibility testing. To evaluate the use of susceptibility testing in guiding IAP choice, we analyzed the subset of large hospitals in our system with comprehensive pharmacy data over the same period. We identified 1038 GBS-positive women who had an uncomplicated vaginal delivery at term. Twenty-six women (3%) received clindamycin for IAP and 19 (2%) received cefazolin. Of those receiving clindamycin, only 10 (38%) had GBS isolates that underwent susceptibility testing. Five of the isolates were documented to be susceptible to clindamycin and erythromycin, and an equal number had documented resistance to one or both agents.

Discussion

The implementation of CDC IAP guidelines has significantly decreased the incidence of early-onset GBS disease in the United States.¹¹ The rising incidence of clindamycin resistance among GBS isolates, along with inconsistent adherence to CDC susceptibility testing guidelines, threatens infants born to mothers reporting penicillin allergy. The case reported here documents the risks to infants when clindamycin is used for IAP in the setting of clindamycin resistance.

Clindamycin resistance among GBS isolates is increasing. In a 10-year study at Duke University, clindamycin resistance increased from 4% to 10%.¹² More recent US studies have reported resistance rates of up to 33%.^{6,8,9} National data from The Surveillance Network (TSN) database (Eurofins Medinet USA, Inc., Chantilly, Virginia) for 2007 showed a resistance rate among GBS isolates of 28.2% for clindamycin and 36.5% for erythromycin. Our own data demonstrated clindamycin and erythromycin resistance of 24% and 44%, respectively, when all maternal GBS isolates with susceptibility test results were analyzed, and 50% resistance to one or both agents among women who received clindamycin for IAP.

Susceptibility testing is currently recommended only for GBS isolates from women with a history of penicillin allergy at high risk for anaphylaxis.³ A review of laboratory practices¹³ showed that 93% of surveyed laboratories had the capability to report susceptibility testing of GBS isolates and that 83% of these performed testing based on physician request or documentation of penicillin allergy. Despite this, 34% of laboratories did not request such documentation on the laboratory order forms.¹³ A recent systematic study of IAP in penicillin-allergic patients showed that only 11% of patients' isolates had susceptibility testing performed, however 83% received clindamycin as IAP.¹⁰ The reasons for inconsistencies in testing were not evaluated.

The actual risk to the infant of failed prophylaxis when clindamycin is used for an isolate determined in vitro to be resistant is stated in the CDC guidelines as "unclear,"³ and there are few published reports. One report documented perinatal disease, but without isolates available for susceptibility testing.¹⁴ One other report documented perinatal GBS infection with a resistant isolate despite clindamycin prophylaxis.¹⁶ In conjunction with these prior publications, our case demonstrates failure of prophylaxis with clindamycin when isolates are resistant.

In this study, we did not address adherence to CDC guidelines recommending the use of cefazolin for IAP for patients reporting penicillin allergy not at high risk for anaphylaxis.³ Although up to 10% of pregnant women can be expected to report a penicillin allergy,¹⁵ rates of anaphylaxis are significantly lower (1 to 5 cases per 10 000 drug courses). The nature of the penicillin allergy was not documented in our case report, as is common.¹⁰ Without documentation of the type of penicillin allergy, clindamycin may be chosen for IAP even though cefazolin might be a safe and more effective alternative. In our hospital data set, fewer women received cefazolin than received clindamycin.

Our data and literature review indicate that clindamycin continues to be used for IAP in the absence of susceptibility testing. With resistance to clindamycin increasing, the likelihood of providing inadequate IAP is also increased. Although further study is necessary to fully quantify the costs and the risks associated with inadequate clindamycin IAP, we suggest that there are indications for considering either regular susceptibility testing or improved processes for documenting and reporting penicillin allergy to laboratories. Further, physicians should be encouraged to use cefazolin for IAP whenever appropriate.

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Glossary

CDC	Centers for Disease Control and Prevention
GBS	Group B <i>Streptococcus</i>
IAP	Intrapartum antibiotic prophylaxis

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