Vancomycin Crosses Placental Barrier, Study Finds

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MONTEREY, CALIF. — The first in vivo study of the pharmacokinetics of IV vancomycin in pregnant women found that it crosses the placental barrier, and that the dose recommended for prophylaxis against neonatal group B streptococcus infection may be too high, Dr. Joann Laiprasert said.

Penicillin is the first-line choice for prophylactic treatment of pregnant women colonized with group B streptococcus (GBS) at 35-37 weeks' gestation. For women with penicillin allergy who have a high risk for anaphylaxis, clindamycin is the preferred drug, but 15%-30% of GBS isolates are resistant to clindamycin. Erythromycin should not be used in this situation because it has a similar resistance pattern and its passage through the placenta is incomplete.

Vancomycin is recommended for pregnant women at high risk of anaphylaxis from penicillin who have clindamycin-resistant GBS, she explained at the annual meeting of the Infectious Diseases Society for Obstetrics and Gynecology.

In the study, 13 healthy pregnant women with no indications for antibiotics volunteered to receive 1 g of intravenous vancomycin. Seven women (54%) did not get the full dose because they developed symptoms of Red Man's syndrome, and the drug was stopped. Despite not getting the full dose, all women and fetuses had serum levels of vancomycin above the 1 mcg/mL breakpoint for effective prophylaxis against neonatal GBS, reported Dr. Laiprasert of the University of Michigan, Ann Arbor, and her associates.

The investigators extrapolated the data to model the effects if all women had received 1-g doses and calculated that this would produce supertherapeutic serum levels of the drug in the mother and the fetus. A second model in which all women received only 500 mg of vancomycin still would have resulted in therapeutic levels in maternal and fetal compartments.

The first four women in the study received the drug in 60-minute infusions, and an interim analysis found that three of them (75%) developed symptoms of Red Man's syndrome: pruritus, shortness of breath, rash, or hypotension. For the following nine patients, the infusion duration was lengthened to 90 minutes, and four of them (44%) developed symptoms of Red Man's syndrome.

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One woman required treatment with saturated oxygen after developing a moderately severe reaction with symptoms of hypotension, shortness of breath, and oxygen desaturation. Investigators stopped the study after that, with enough data to draw conclusions about vancomycin's pharmacokinetics. Therapeutic drug levels were seen in fetal serum within 30 minutes after completing the 90-minute infusion (120 minutes after starting the infusion) and persisted for 8 hours.

Because less than the recommended 1-g dose of vancomycin produced therapeutic serum levels and because Red Man's syndrome was so common, a 500-mg dose should be considered adequate, Dr. Laiprasert suggested. A slower infusion rate also may be important for safe administration of vancomycin during pregnancy. Redosing vancomycin at 12-hour intervals seems reasonable if needed, she added.

The investigators collected amniotic fluid samples and plan to study them to improve understanding of the metabolism of vancomycin in the fetal circulation.

Dr. Mark D. Pearlman, one of Dr. Laiprasert's associates in the study, commented after her talk that using a lower dose of vancomycin in these patients makes sense. Other treatment options also need to be studied for women with clindamycin-resistant GBS who are at high risk for anaphylaxis from penicillin, added Dr. Pearlman of the university.

"We really need to pressure the FDA and others to start to look at other non–β-lactams that are active against GBS, to have alternatives to vancomycin," he said. "There are a whole host of newer, extended-spectrum, gram-positive drugs that have great activity against clindamycin-resistant GBS." ■

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