Antibiotic Concentration in Maternal Blood, Cord Blood and Placental Tissue in Women with Chorioamnionitis

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Introduction
Acute chorioamnionitis or intra-amniotic infection remains an important disease entity in obstetrics, and with an incidence of approximately 1-3% of all pregnancies, it remains an important contribution to maternal and perinatal morbidity [1, 2]. Although recent information has emphasized the need for immediate antibiotic therapy once the diagnosis is made [3,4], there is no unanimity of opinion on the ideal antibiotic regimen to treat the infection. Many antibiotic regimens have been used in the treatment of chorioamnionitis, but little is known regarding the antibiotic concentrations in the fetus and placental tissues. We have previously published data regarding the levels of several different antibiotics in maternal and cord blood, as well as in placental tissue [5]. The purpose of the present study was to ascertain the concentrations of several relatively new broad-spectrum antibiotics in maternal and fetal blood and placental tissue. These new antibiotics might prove clinically useful for the treatment of acute chorioamnionitis.

All antibiotic assays were determined using high-pressure liquid-chromatography methods as previously described [3]. All assays were done using UV detection at wavelengths of 229 nm for β-lactam antibiotics, and 313 nm for the β-lactamase inhibitors. Prior to assay, all β-lactamase inhibitors were derivatized with imidazole. Instruments used were a Waters 481 detector, an autosampler and a 10-MV recorder. All procedures were validated and had a coefficient of variation of less than 10 % and recoveries of greater than 90 %, as calculated by linear least-squares regression analysis.

Results
The results of the antibiotic penetration studies are summarized in table 1. All three antibiotics were found in cord blood and placental tissue. Both ampicillin-sulbactam and cefotaxime achieved equal levels in maternal and cord blood (ratios of cord to maternal blood were approximately 1.0). Ticarcillin-clavulanic acid cord to maternal blood ratios were about 25%
lower (0.7) than the above two antibiotic regimens. Ampicillin-sulbactam and ticarcillin-clavulanic acid had almost identical placental tissue to maternal blood drug ratios, while that for cefotaxime was almost 50% lower (0.2).

Materials and Methods
Pregnant women at 37 weeks’ gestation or greater with the diagnosis of chorioamnionitis were included in the study. All women had temperatures of 38 °C or higher, and all received their antibiotics while in labor. Blood specimens were collected immediately at delivery, centrifuged, and the serum frozen at – 70 º C until analysis. In addition, samples (10 g) of fetal placental tissue was collected at delivery and frozen until analysis.

Discussion
Data from the present study indicate that all antibiotics tested penetrated into cord blood and placental tissue. In a previous study [5], we measured maternal blood, cord blood, and placental tissue concentrations of clindamycin, mezlocillin, ampicillin, cefoxitin, and gentamicin, and found that all crossed the placenta. Ampicillin and gentamicin had the highest cord to maternal blood ratios. In the present study, ampicillin-sulbactam and cefotaxime had the highest cord to maternal blood ratio. However, ticarcillin-clavulanic acid was also found in measurable amounts in both cord blood and placental tissue. With the recent reports [3, 4, 6] recommending intrapartum treatment of women with chorioamnionitis, it is imperative that the antibiotic achieve measurable levels in the fetus and placental tissues. Therefore, we conclude that the broad-spectrum antibiotics studied penetrated the fetal placental tissues and, in this regard, may be considered adequate for achieving fetal levels. Clinical efficacy studies are needed, however, to compare whether the broad-spectrum antibiotics are ideal in the treatment of intra-amniotic infection from both the maternal and newborn standpoints.

References

Maberry/Trimmer/Bawdon/Sobhi/Dax/ Gilstrap
Maternal Fetal Blood Antibiotic Concentration