INFECTIOUS DISEASE

Abstracts 18 – 26

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18 Transplacental passage of vancomycin from mother to newborn

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OBJECTIVE: There is limited data on vancomycin use in labor and transplacental drug passage. Two ex vivo placenta perfusion studies demonstrated minimal transfer. 16 total patients from 3 other studies reported maternal and cord blood values at delivery and showed transplacental passage but 14 were subtherapeutic. Therapeutic trough range is 10-40 mcg/ml. Our study objective was to evaluate a larger number of patients using the standard dosing and then modify dosing (if needed) to attempt to reach therapeutic levels.

STUDY DESIGN: Every mother that entered labor with a positive GBS culture and a high risk penicillin allergy with GBS resistance to clindamycin or unknown sensitivity was consented. Patients received the standard 1 gram IV dose Q 12 hours which was then changed to 15 mg/kg IV Q 12 hours after initial data analysis showed subtherapeutic levels in mother and neonate. Maternal vancomycin levels obtained at delivery were compared with cord blood values.

RESULTS: 43 patients were consented with 31 receiving the standard 1 gram dosing and 12 receiving the 15mg/kg dosing. For standard dosing, 10 mothers (32%) had therapeutic levels at delivery but only 3 cord blood values (10%) were therapeutic. With 15 mg/kg dosing, 6 mothers (50%) had therapeutic levels at delivery and 4 cord blood values (33%) were therapeutic. 15 patients delivered >8 hours after the last dose and all but 1 were subtherapeutic. Of the 16 therapeutic mothers, all but 2 occurred when delivery was <6 hours after dosing. Of the 27 subtherapeutic mothers, the last dose to delivery was >6 hours in 23 (85%). In patients with a BMI >30, only 27% in the standard dosing group had therapeutic levels versus 60% that were therapeutic in the 15 mg/kg dosing group.

CONCLUSION: With standard dosing, only 10% of neonates have therapeutic levels at delivery. The pharmacologic pattern shows that transplacental passage occurs with fetal levels equaling maternal levels but transplacental transport is somewhat slow in both directions. Further study examining alternate dosing and frequency is needed.

19 Alcohol inhibits innate anti-HIV factor expression and enhances HIV infection of cord blood monocyte-derived macrophages (CBMDM)

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OBJECTIVE: Approximately 6,000 to 7,000 HIV-infected women give birth each year in the United States, resulting in 280 to 370 new perinatal infections, despite the wide availability of potent antiretroviral treatment. In adult, non-pregnant, populations alcohol abuse has been implicated as a co-factor in HIV infection and progression. In vitro investigations have shown that alcohol enhances HIV infection of monocyte-derived macrophages and lymphocytes. We hypothesize that alcohol may similarly increase the risk of perinatal HIV transmission through a decrease in innate anti-HIV factors and a parallel increase in the susceptibility of monocyte-derived macrophages to infection.

STUDY DESIGN: Fresh cord blood was collected from uncomplicated term deliveries. Fresh monocytes were isolated, then in vitro cultured for 7 days for macrophage differentiation. Afterwards were incubated with or without alcohol .RNA was extracted and real time PCR performed for anti-HIV microRNAs, tetherin, APOBEC3G and APOBEC3H, IFN and RIG-I.

RESULTS: Alcohol pre-treatment of CBMDM significantly inhibited the expression of several key HIV restriction factors: anti-HIV microRNAs, tetherin, APOBEC3G and APOBEC3H. In addition, alcohol suppressed the expression of IFN regulatory factor 7 (IRF-7) and RIG-I, the critical modulators in IFN pathway. The suppression of these innate restriction factors was associated with reduced production of type 1 IFNs and the enhancement of HIV infection of CBMDM.

CONCLUSION: Our findings suggest that maternal alcohol consumption may facilitate HIV infection/replication, promoting vertical transmission of HIV.