

Session 107. POSTER
HIV & AIDS: Pediatrics/Maternal
Saturday, 12:30 p.m. - 2 p.m.

427 Use of Specific Combination Antiretroviral Therapies for Prevention of Perinatal HIV Transmission (PHT): Pediatric Spectrum of HIV Disease Project (PSD) U.S.A.; 1995-2001

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Background: Combination antiretroviral therapy (CT) is recommended in pregnancy for prevention of PHT. However, there is no recommendation on the preferred CT combination agents, and the pattern of prenatal CT usage in clinical practice is unknown. We studied trends in CT use in HIV-infected pregnant women and its impact on PHT. Methods: We analyzed PSD data that were collected prospectively by medical record review of HIV-exposed infants in 8 areas of the U.S. born between 1995 and 2001. We included only infants with known HIV infection status and maternal CT use in the final analysis. Maternal viral load and CD4 count data were not collected during this period. Results: 7035 HIV-exposed newborns were identified. From 1995-2001, there was a marked increase in the use of maternal CT (1.34% to 79.77%). The 5 most common classes of CT agents used and the associated risk of PHT are as below. The commonest agents used were: NRTI = ZDV, 3TC; NNRTI = nevirapine; and PI = nelfinavir. There was a significant incremental benefit in reduction of PHT among groups 'none', 1 NRTI and 2 NRTIs (dual CT). There was also a trend towards superiority of triple CT as compared to dual CT (P = 0.09). Triple CT consisting of 2 NRTIs and either 1 PI or 1 NNRTI were comparable in efficacy. Delivery by cesarean section vs. vaginal route did not influence the outcome of PHT. Conclusion: CT rates increased substantially from 1995-2001. PHT decreased with CT as the number of CT agents increased. Further studies are needed which can take into account the reasons for the choice of CT, maternal viral load, CD4 counts and indications for C-S. These results document the continued U.S. progress in reducing perinatal transmission.

	None	1 NRTI*	2 NRTIs**	2 NRTIs + 1 PI	2 NRTIs + 1 NNRTI
Infected	495 (24.17%)	163 (8.07%)	24 (4.72%)	19 (3.38%)	3 (1.62%)
Uninfected	1553	1857	485	543	182

(NRTI = nucleoside reverse transcriptase inhibitor; NNRTI = non-NRTI; PI = protease inhibitor) * None vs. 1 NRTI, P < 0.001; ** 1 NRTI vs. 2 NRTIs, P = 0.013

428 Nelfinavir-Induced Glucose Intolerance in Pregnancy: Placental and Fetal Outcomes in Rats

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Background: The use of PIs is associated with glucose intolerance (GI). Maternal GI of gestational diabetes (GD) is associated with maternal-fetal complications. We investigated the placental (PL) and fetal outcomes in utero following administration with NFV in rats. Methods: A total of 21 female Sprague-Dawley rats were randomly assigned to a control (C), low dose (LD) NFV (100 mg/kg/day) or high dose (HD) NFV-treated (400 mg/kg/day) group. Rats were mated during an overnight 12-hr period. Sperm-positive vaginal smears denoted day 0 of pregnancy. Necropsy was performed on all females at day 20 of gestation. The placentas and fetuses were isolated, weighed and measured. Fetal livers (FL) were removed and weighed. Maternal non-fasting plasma glucose (NFBG) levels were determined. Two veterinary pathologists performed histology reviews in a blinded-manner. Data were analyzed by ANOVA, post hoc testing by the method of Tukey and with significance set at p < 0.05. Results: Necropsy was performed on 7 C (total of 100 concepti), 8 LD (total of 118 concepti) and 6 HD NFV-treated (total of 77 concepti) dams. The mean (± SEM) PL weight ratios were 0.49 ± 0.005 gms, 0.53 ± 0.005 gms and 0.52 ± 0.008 gms in C, LD and HD NFV-treated groups, respectively (p < 0.001). The PL surface area (SA) was significantly larger in the LD and HD NFV-treated groups as compared to C, 1.52 ± 0.012 cm², 1.55 ± 0.017 cm² vs. 1.45 ± 0.015 cm², respectively (P < 0.05). A significantly lower FL to weight ratio was observed in the LD and HD NFV-treated groups as compared to C, 0.081 ± 0.001 gms, 0.081 ± 0.002 gms vs. 0.097 ± 0.001 gms respectively (p < 0.001). No differences were noted for fetal weights, sizes or maternal NFBG among the treatment groups. A mild to moderate diffuse congestion, multifocal telangiectasia and myeloid and erythroid hyperplasia were observed for all FL in both LD and HD NFV-treated dams. Conclusions: Our data suggest the alterations in PL weight and SA and FL weight ratio are consistent with clinical and experimental model of GD, despite a lack of difference in maternal NFBG. Observational safety studies are needed in newborns to determine if hepatic abnormalities may develop with exposure to NFV in utero.

429 Perinatal Transmission of HIV Infection: Preliminary Results of a Vertical Transmission Prevention Program (AMAPES)

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Background: In Argentina vertical transmission (VT) accounts for 6.5% of total AIDS cases and 95% of pediatric cases. The government provides diagnostic tests, antiretroviral drugs and formula for VT prevention (VTP). Discontinuous provision of supplies, delayed tests results and poor education of health care providers conspire against the efficacy of this program. The "Asociacion de Caballeros Argentinos de la Soberana Orden Militar de Malta" provided financial support to carry out AMAPES Program to optimize VTP in public hospitals. Objective: To evaluate the impact of AMAPES program. Methods: AMAPES was started in Aug 01 at 3 institutions assisting 12,000 births annually with 1% HIV seroprevalence in pregnant women (PW). Specific needs were evaluated at each hospital before inclusion. The main problems found were insufficient laboratory determinations, inadequate counseling and identification of HIV + PW, and lack of updated guidelines. AMAPES provided human and material resources, professional counseling and supervision. PW were managed according to the 2001 CDC Guidelines. Results: Up to May 02, 109 HIV + PW were detected (1.2% seroprevalence): 55/109 (50%) were diagnosed during pregnancy. 77% were evaluated with viral load (VL) and 72% with CD4; 57% of these determinations were performed by AMAPES. ZDV was indicated to 42/109 (38%) PW after evaluation according to PACTG 076; HAART to 35/109 (32%) and ZDV+3TC or NVP to 9/109 (8%) with late prenatal control. 65/109 PW gave birth to 66 newborns: 21/65 (32%) had vaginal births and 44/65 (68%) had cesarean sections (CS). In 46% (30/65) VL was repeated at term to help decide the mode of delivery; 18/30 (60%) had VL < 1000 cp/ml; 17 had CS. CS was less in PW re-evaluated with VL at term: 56% (17/30) vs. 71% (25/35). AMAPES average costs per PW were US\$ 50. No VT was documented in the 23 newborns evaluated. Comments: AMAPES improved identification of HIV + PW, extended laboratory evaluation and lowered the number of CS in adequately evaluated PW. Programs like AMAPES are a good complement to government actions in countries where health resources are discontinued due to economic reasons.

430 Perinatally Acquired HIV-1 Infection - Lipid Abnormalities Associated with Treatment with Protease Inhibitors

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Treatment of HIV-1 infection of adults with protease inhibitors is associated with hyperlipidemia. However, data on this association for children treated with protease inhibitors are limited. To determine the frequency of hyperlipidemia for perinatally infected children we analyzed data from 53 followed by the University of Texas Pediatric HIV Clinic. Thirty nine of these patients were receiving a protease (PI) containing regimen (plus nucleosides and/or non-nucleosides) and 14 were on double or triple antiretroviral therapy including nucleosides and non nucleosides (NPI). The groups were very similar in age (mean 7.4 versus 7.5, range 2 to 16 years old), CD4 (28% versus 26%, range 8% to 50%), and viral load (log10; 3.6 versus 3.5, range undetectable to 6.4) for PI and NPI, respectively. Cholesterol was significantly increased (>171 mg/dl) for 54% of PI patients as compared to 21% of NPI patients (p < 0.04). Triglycerides were increased (>135 mg/dl) in 51% PI versus 21% NPI (p < 0.06). The mean triglycerides concentration was also significantly elevated for the PI group (mean 173 versus 106 mg/dl, p < 0.03). HDL was significantly lower in the PI group (mean 46 versus 68 mg/dl, p < 0.02). LDL was higher in the PI group (mean 96 versus 72 mg/dl, p < 0.11). Of the 39 patients on PI regimens, 22 were receiving nelfinavir and 12 lopinavir/ritonavir. Fifty five percent versus 58% of recipients of the respective regimens had significantly increased levels of cholesterol. However the regimens differed markedly in elevated levels of triglycerides; 32% versus 92%, p < 0.002. Protease inhibitor treatment of perinatally acquired HIV-1 infection associates with hyperlipidemia in many treated children. The rates approximate those seen in adults. The pattern of hyperlipidemia may be a function of the PI treatment regimen.

431 Does Poor Maternal Adherence Contribute to Selective Transmission of Multi-Drug Resistant HIV to the Newborn: A Case Study

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Perinatal HIV infection occurs in 2-5% of exposed babies, despite standard prevention guidelines. We describe a baby born with a multi-drug resistant virus (MDR). The mother was known HIV positive for 5 years prior to pregnancy. Anti-retroviral therapy (ART) included AZT/3TC/NVP with poor adherence in the past. She stopped ART when she became pregnant. She first sought medical care at 20 weeks gestation. Viral load (VL copies/ml) was 11900. She restarted AZT/3TC/NVP, was intermittently adherent, but better than before. VL < 400-24 wks, 459-32 wks, 968-34 wks. She & the baby received AZT prophylaxis. The baby was diagnosed with HIV infection by ELISA & HIV DNA PCR positive x 2. The mother continued AZT/3TC/NVP, remaining poorly adherent. Genotyping on mother and baby are shown. Results: This baby was born infected with a MDR virus, however, genotyping on the mother postpartum revealed a strain that remained sensitive. The inconsistent maternal adherence led to the emergence of a resistant strain & this strain, not the wild-type virus (WT) infected the fetus. In this case, standard perinatal prophylaxis probably suppressed WT but failed to prevent the transmission of the MDR strain. At 7 months postpartum the mother was beginning to show the reemergence of WT strain with no detection of the MDR strain that had infected the baby. Repeat genotype after 2 1/2 years of inconsistent therapy in the mother showed re-emergence of strains resistant to NNRTIs. Conclusions: Perinatal transmission does occur despite best efforts to reduce perinatal transmission using current recommendations. It leads to the baby being infected with a MDR virus from the mother as a result of poor adherence. The degree of resistance will depend on prior treatment history, current treatment & viral fitness of the resistant strain.

	GENOTYPING RESULTS			
	Viral load	Current Treatment regimen	RT mutations	Protease mutations
Baby age 6 months	443606	none	K103N (all NNRTI) M184V (3TC, FTC, ddC, ABV)	L33V odd (RTV) L63V odd (DDV, NFV)
Mother 7 mo postpartum	10756	none	None	L33V L63V
Mother 2 1/2 yrs postpartum	33670	AZT/3TC/EFV inconsistent adherence	K103N (all NNRTI)	L33V L63V