HIV and Pregnancy

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SPEAKER DISCLOSURE INFORMATION

GRAND ROUNDS: "_HIV and Pregnancy__"

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I have a financial relationships to disclose: Orasure Technologies

Objectives

- Review antepartum concerns and counseling for HIV infected pregnant women
- Review antepartum, intrapartum and postpartum treatment of HIV infected mothers

HIV & Pregnancy Pathogenesis

	Transmission Risk	**Intervention**
Pregnancy	10-25%	ART during pregnancy
Labor & Delivery*	35-40%	Intrapartum Zidovudine
Breastfeeding	35-40%	Breastfeeding Contraindicated

* One study estimated 92% infections currently in the last 2 months, with 65% Intrapartum

Transmission

- Transmission is more common in preterm births and increased duration of rupture of membranes
- More advanced disease is also linked with higher transmission rates
- More advanced disease can be measured clinically by the presence of AIDS defining conditions, lower CD4 counts, or high plasma HIV RNA levels

Treatment During Pregnancy

- Antiretroviral therapy in pregnancy involvesseparate but related goals
  - Treatment of maternal HIV disease
  - Minimizing maternal and neonatal side effects
  - Reduction of perinatal transmission, also called
    - Vertical transmission and
    - Mother to Child Transmission (MTCT)

Treatment Facts

- In the United States, approximately 7000 HIV-infected women give birth annually
- Without any intervention to reduce transmission, 1750 newly infected babies would be born every year
- In 1994, Pediatric AIDS Clinical Trials Group (PACTG) protocol 076 showed that a three-part regimen of zidovudine (ZDV) administered during pregnancy, labor and to the newborn, could reduce the risk of perinatal transmission by nearly 70 percent
- Combination of elective cesarean section and receipt of ZDV during the antepartum, intrapartum and neonatal periods reduced transmission by about 85 percent compared to other modes of delivery and no antiretroviral therapy

ZDV Mechanism of Action

- Reduction in maternal antenatal viral load
- Restriction of HIV replication in the placenta
- Pre and postexposure prophylaxis of the neonate
- Mild, reversible anemia in the infant seen during the first 6 weeks of life
- No pattern of abnormalities in amniotic fluid volume or fetal growth and development

Initial HIV OB Evaluation

- Discussion regarding risks and benefits of therapy for the mother during pregnancy and labor and for the newborn for six weeks after birth. ADHERENCE!!
- Review HIV history, current and prior medications (how long, why stopped), CD4 nadir, use of medication being taken to prevent opportunistic infections and prior resistance testing—in conjunction with HIV medicine
  - Pneumocystis carinii pneumonia – trimethoprim/sulfamethoxazole (TMP/SMX) or pentamidine in the first trimester to avoid teratogenicity
  - Mycobacterium avium complex – azithromycin

HIV Antiretroviral Counseling

- No treatment at all—**25%** risk of transmission
- ZDV alone (ante/intra/post) will decreased rate of transmission to **5-8%** (no longer recommended 2nd to drug resistance).
- Combination antiretroviral therapy antepartum (with ZDV intra and post) will decrease transmission **<2%.**
- If VL >1000 at term (or time of delivery), scheduled C section at 38wks.

Combination Antiretroviral Therapy

- Combination antiretroviral therapy, using 3-4 drugs from 2 or more classes, usually consisting of two nucleoside analog reverse transcriptase inhibitors and a protease inhibitor, is the recommended standard treatment for HIV-1 infected pregnant women and adults
- Ideally want regimen to include ZDV during pregnancy, unless resistance or severe toxicity

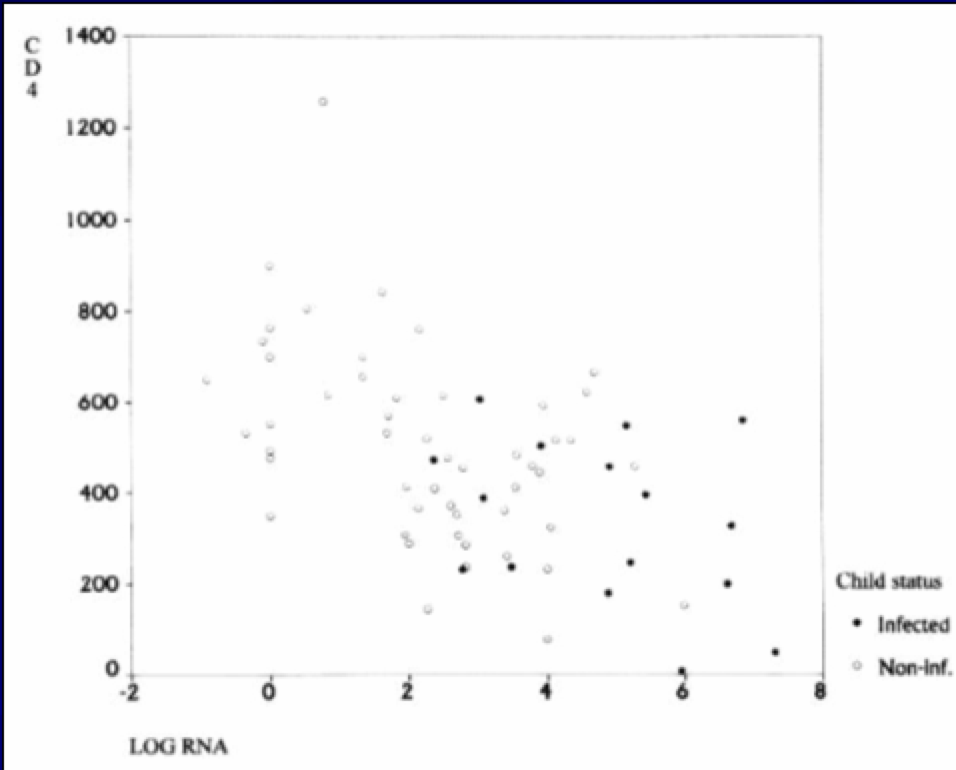
Combination Antiretroviral Therapy

- Women receiving HAART regimens that reduce HIV-1 RNA to <1,000 copies/mL or undetectable levels have very low rates of perinatal transmission
- However, since transmission can occur at low or undetectable HIV-1 RNA copy numbers, RNA levels should NOT be a determining factor when deciding whether to use HAART for chemoprophylaxis

Maternal Transmission

Era	Treatment	Outcome
pre-1996 (or developing country)	No therapy	28%
Monotherapy	AZT prenatal, intrapartum and postpartum	7%
Dual Therapy	2 antiretrovirals with AZT intrapartum and post partum	<2%
Triple Therapy Non-PI PI	3 or more antiretrovirals with AZT intrapartum and post partum	1%

Relationship between HIV-1 RNA load and CD4 count for transmitting and nontransmitting mothers



Key
•infected child o uninfected child

NO relationship between VL and HIV transmission

Vertical HIV-1 Transmission Correlates with a High Maternal Viral Load at Delivery.
Coll, O; Hernandez, M; Boucher, C; Fortuny, C; de Tejada, B; Canet, Y; Caragol, I; Tijnagel, J; Bertran, J; Espanol, T

Journal of Acquired Immune Deficiency Syndromes & Human Retrovirology. 14(1):26-30, January 1, 1997.

HAART Scenarios

- 1) No prior HAART/ARV naive
  - Get GAART prior to starting
  - If for patient own health, start combination ARV ASAP. If not, may wait until 2nd trimester to minimize nausea and vomiting
  - No AZT alone
- 2) Prior HAART
  - Get full medication history (which drugs, why stopped, prior infections/prophylaxis)
  - Get GAART prior to starting HAART
- 3) Currently on ARV/HAART
  - If VL maximally suppressed, continue regimen (unless EFV—risk of NTD)
  - If detectable VL, check GAART and change regimen.

Antiretrovirals

- Commonly used in pregnancy:
  - NRTIs—nucleoside reverse transcriptase inhibitors
  - NNRTIs—non-nucleoside reverse transcriptase inhibitors
  - PIs—protease inhibitors

  - Others: Entry inhibitors (maraviroc), Integrase inhibitors (raltegravir)—minimal data about use in pregnancy

Common Antiretrovirals

- Lamivudine, zidovudine—together Combivir**
  - (abacavir, emtricitabine)
- Nevirapine (if CD4<250 otherwise hepatic toxicity)
- Lopinavir/ritonavir—Kaletra**
  - (nelfinavir, saquinavir)

**commonly used

Short Term Side Effects

1) Hepatotoxicity—NRTIs, NNRTIs, PIs
   - Fatigue, jaundice, hepatomegaly, nausea and vomiting
   - Increased risk if HBV/HCV coinfection, elevated LFTs, alcohol use
   - Check LFTs
2) Hyperglycemia—PIs
   - Polyuria, polydipsia, polyphagia
   - Increased risk if overweight, HCV, family history or diabetes
   - Check Glucose, early GTT
3) Lactic Acidosis--NRTIs
   - Low pH and increased Acid
   - Increased risk if overweight, female, pregnant, HCV
   - Check Chem 10, LFTs, lactate, pH

Long Term Side Effects

1. Hyperlipidemia—PI
2. Lipodystrophy
3. Osteonecrosis
4. Skin rash

Stopping Antiretrovirals

- If stopping medications during pregnancy:
  - Stop NNRTI 1st, then others 7d later
  - If nausea/vomiting or toxicity, first try treating side effect (if normal labs). If not effective, stop all medications together and restart all together.

Monitoring during Pregnancy

- CD4 q3months
- VL 1st visit and q4wks while changing meds or until VL undetectable
- If elevated VL—GAART
- SE monitoring—CBC, LFTs, Chem 10
- Early GTT esp if obese, PI use
- 1st trimester sono dating
- 2nd trimester anatomy
- Additional fetal monitoring controversial

Recommended Mode of Delivery

- ACOG recommends consideration of scheduled cesarean delivery at 38wks for HIV-1 infected pregnant women with HIV-1 RNA levels >1,000 copies/mL near the time of delivery, regardless of the type of antiretroviral therapy the women is receiving
- In women at very low risk for transmission, such as those with low or undetectable viral loads, the additional benefit provided by elective cesarean section may be marginal and increased risk of infectious complications post partum
  - If vaginal delivery is chosen, AROM and invasive procedures that may cause a break in the infants skin should be avoided

Mode of Delivery

- ZDV intrapartum prophylaxis should be provided, regardless of the mode of delivery
  - During labor, IV administration of ZDV in a 1 hour initial dose of 2mg/kg, followed by a continuous infusion of 1mg/kg/hr until delivery, for ideally 3hrs prior to delivery
- Other antiretroviral medications taken during pregnancy should not be interrupted near the time of delivery, regardless of route of delivery

Mode of Delivery

- Management of women originally scheduled for cesarean delivery who present with ruptured membranes must be individualized based on duration of rupture, progress of labor, plasma HIV-1 RNA level, current antiretroviral therapy and other clinical factors
- The longer the time since the membranes ruptured, the greater the percentage of eventual transmissions that will have occurred before a surgical procedure can be undertaken
- Avoid Methergine if taking PI or Efavirenz—may cause exaggerated vasoconstriction

Other Treatment Options

- There are several antiretroviral regimens that when started during labor and given to the newborn may reduce the risk of mother to child transmission even for women who have not received antiretroviral treatment during pregnancy
- While not as effective as the full 3-part ZDV PACTG 076 regimen, they are better than not getting any drugs to reduce transmission

Infants

- Check a CBC prior to administration of ZDV
- Repeat testing of CBC following completion of 6-week ZDV regimen and at 12 weeks of age
- Screened for HIV infection at birth, 2 weeks, 1-2 months and 3-6 months of age, looking for HIV DNA
- Prophylaxis for PCP (bactrim) should be started following completion of ZDV therapy at 6 weeks of age

ZDV: Infants

- Oral administration of ZDV to the newborn (ZDV syrup at 2mg/kg/dose Q6hr) for the first 6 weeks of life, beginning at 8-12 hours after birth
- IV dosage for full-term infants who cannot tolerate oral intake is 1.5mg/kg IV Q6hr

Postpartum Evaluation

- Newly diagnosed HIV+ patients or patients not receiving care during pregnancy should be referred to ID services for HIV follow up post partum
- When combination therapy during pregnancy was required for treatment of the women's HIV disease, patient should continue medications after delivery.
- If patients were on HAART to prevent vertical transmission, review with the HIV clinician prior to delivery whether to stop medications after delivery.

Postpartum Evaluation

- Maternal medical services during the antepartum and postpartum period need to be coordinated between obstetric and HIV-specialist health care providers
- Comprehensive care and support services are required for infected women and their families – HIV-related medical care, psychosocial support and assistance, contraceptive use, medication adherence and disclosure
- If C section, patients are at increased risk of wound infection and poor healing that is increased with low CD4 counts.

Resources

WEBSITES:

aidsinfo.nih.gov

cdc.gov/hiv/

aids.gov

acog.com

Phone:

Perinatal Hotline *888-448-8765*