Prevention of Perinatal HIV Transmission: The US Experience

Sunanda Gaur MD
ACTG 076: Results

Transmission Rate (%)

Placebo
n= 184
22.6%

ZDV
n= 180
7.6%

66% reduction in risk of transmission (P = <0.001)
Mother to Child HIV Transmission in the US over Time

- 1993: WITS
- 1994: PACTG 076
- 1997: PACTG 185
- 1999: WITS
- 2001: PACTG 247
- 2002: PACTG 316

HAART USE
Estimated AIDS cases in children
US 1992 - 2005

Year of Diagnosis

Number of cases


894 879 799 663 509 329 241 187 127 118 104 67 47 58

0 100 200 300 400 500 600 700 800 900 1000

Number of cases

Year of Diagnosis
Lessons Learned - 1

- Key elements for maximal reduction in HIV transmission from mother to infant are:

  ✓ Maximal viral suppression by HAART therapy in pregnancy

  ✓ Use of Elective C section if maternal VL remains >1000 copies/ml by 36 weeks of gestation

  ✓ Three part ZDV regimen (prenatal, intra-partum and neonatal) is instituted regardless of viral load

  ✓ Breast feeding is avoided
Lessons Learned - 2

Less than optimal interventions can also make a difference!!
Short Course Therapy Options Guidelines: USA

- Intrapartum IV AZT+ 6 weeks AZT for newborn
- AZT+3TC in labor & 1 week AZT+3TC for newborn
- 1 dose NVP labor onset & 1 dose NVP for newborn at 48 hours of age
- Single dose maternal/newborn NVP regimen + intrapartum IV AZT + 6 weeks infant AZT
- If NVP used alone or in combination with AZT, consider maternal AZT/3TC intrapartum and continue 3 – 7 days postpartum to reduce NVP resistance

PHS task force 10/06  http://AIDSinfo.nih.gov
NJ Pediatric HIV/AIDS Cases & Exposures 1993 – 2005

No. of children born to HIV positive mothers

Yr. of birth

HIV negative  HIV positive

0 50 100 150 200 250 350 400

93 94 95 96 97 98 99 00 01 02 03 04 05

21% 17% 15% 14% 12% 8% 6% 6% 5% 2% 4% 3.5% 2%
PERINATAL COLLABORATIVE PROGRAM

HIV infected pregnant woman

RWJAP

HROB MFM

Multidisciplinary Team

Labor and Delivery

Neonatal

Healthy Newborn

Healthy Newborn
Ongoing HIV transmission: US

• Approximately 350-400 new pediatric HIV infections occur each year

• Perinatal HIV transmission rate in the US ranges between 2-5%
Where are the missed opportunities?

How can we eliminate residual perinatal HIV transmission?
MISSED OPPORTUNITIES
CASE # 1

A 14 month old child is referred to rule out HIV infection. Patient’s mother just found out that she is HIV (+) during life insurance screening. She gives no risk factors for HIV.

Mother had prenatal care but was never offered HIV testing. Patient was born at full term. Baby was breast fed for 8 months.

Patient was tested and found to have a (+) HIV DNA PCR (Infected)
Missed Opportunities
Case # 2

Patient’s mother presents to L & D unit in labor. No prenatal care, h/o drug use, HIV status unknown.

Admitting orders:
- HIV Rapid Test, HIV consent in chart.

Progress notes next day:
- VDRL (-);
- No mention of HIV test result.

Baby: on DYFS hold;
- Drug screen positive.
- DYFS places baby with family member.
- No HIV test done

2.0 yrs later, baby tests HIV infected
Patient’s mother presents to L & D unit in labor. Known h/o IV drug use in the past. Partner known HIV (+). Mother was HIV (-) in 1st trimester and had good prenatal care.

Baby born at term. Developed petechiae at age 1 day.

Work up for thrombocytopenia included HIV DNA PCR which was POSITIVE. (Infected)
<table>
<thead>
<tr>
<th>Strategies to increase HIV testing in pregnancy (2003)</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Physician education</td>
</tr>
<tr>
<td>- “Opt out” testing</td>
</tr>
<tr>
<td>- <strong>Third trimester repeat HIV testing</strong> if ongoing risk factors during pregnancy</td>
</tr>
<tr>
<td>- <strong>Rapid HIV testing</strong> during labor and delivery for all women with undocumented HIV status. Rapid test in newborn (within 72 hours) if not done in mother or postpartum rapid test</td>
</tr>
</tbody>
</table>
Patient’s mother went for prenatal care which included HIV test in 1st trimester which was negative. She did not have any HIV risk factors.

Baby admitted at age 14 months with PCP pneumonia

Mother HIV (+).

Baby HIV DNA PCR (+) (Infected)
CDC: Risk factors for Ongoing Perinatal HIV Transmission

- No prenatal care
- No HIV test offered in pregnancy
- Negative test in early pregnancy but continued risk for HIV acquisition during pregnancy
- Non compliance with HIV medication in pregnancy
“Opt Out” Testing

- Studies show that large numbers of women in the general population are unaware of perinatal HIV transmission reduction treatments.
- Rates of testing in pregnancy vary in different regions depending on approach used.
- Testing rates with “Opt in” testing range between 25%–65%.
- “Opt out” testing improves testing rates.
Reducing Intrapartum HIV Transmission: Short-Course Therapy

- **Short Course –Thailand**: Oral ZDV in non-breastfeeding women from 36 weeks and during labor
  Transmission rate: 9% ZDV vs 19% placebo

- **HIV Net 01**: Sd NVP during labor and to infant at 48-72 hours vs. intra-partum course/ 7 days neonatal ZDV in breastfeeding women (Uganda)
  Transmission rate: 12% NVP vs. 21% ZDV

- Other studies suggest addition of NVP regimen to short-course ZDV may further decrease transmission rate (conflicting data)
Reducing Intrapartum HIV Transmission: Short-Course Therapy

- **Petra study**: oral ZDV/3TC in a breastfeeding population (Uganda, S. Africa, Tanzania)
  - Given from 36 weeks, intrapartum, and postpartum to mother and infant x 7 days
    - Transmission rate: 6% ZDV/3TC vs 15% placebo
  - Given intrapartum and postpartum to mother and infant x 7 days
    - Transmission rate: 9% ZDV/3TC vs 15% placebo
DREAM Cohort: Mozambique

- HAART offered to women irrespective of CD4 counts at 25 weeks+ to 6 months post partum (breast feeding +)

- MTCT 1.2 % !! In 171 mother infant pairs
Impact of Resistance in Pregnancy

- Perinatal transmission of resistance is unusual
- Concern that maternal drug resistance will increase risk of perinatal transmission, but no evidence that this is the case
- Maternal response to subsequent ART may be compromised if non-suppressive ART is used (e.g., single-dose nevirapine). More common in case of medications requiring one genetic mutation for resistance and long half life.
Long term Impact of NVP resistance

• The impact resistance mutations on response to therapy and long-term outcomes of the mother and child are under study

• Chi et al (Zambia): 679/6100 women exposed to sd NVP received NVP based ART. No difference in clinical and CD4 response at 6 and 12 months.

• Jourdain et al: Of 286 Sd NVP exposed women started on NVP based HAART, no difference in clinical and CD4 response at 12 months.
Response to ARV after Sd NVP Exposure

- 218 women (112 Sd NVP exposed, 106 placebo exposed) started ARV.
- Virologic failure at 6 months in 5% of placebo exposed vs. 18.4% SD NVP exposed exposed.
- This difference was not apparent when ARV was begun > 6mths post partum.
- 30 infected infants, Sd NVP exposure associated with higher virologic failure with subsequent NVP based Rx.

• Lockman et al NEJM 356;2 2007, 135-147