HIV IN PREGNANCY

Practices for Maintaining Maternal Health and Preventing Perinatal HIV Transmission

Nina K. Sublette, PhD, FNP
University of Tennessee Health Science Center
College of Nursing: Department of Advanced Practice and Doctoral Studies
College of Medicine: Department of Obstetrics and Gynecology

Southeast AIDS Education & Training Center

PERINATAL TRANSMISSION OF HIV

- First reported in MMWR, December 17, 1982:
  - *Unexplained Immunodeficiency and Opportunistic Infections in Infants* – New York, New Jersey, California
- Prior to 1994, MTCT ranged from 16% - 25% in North America and Europe and up to 45% in developing countries
- Infant's risk of infection increased with mother's illness
  - Advanced CDC disease stage
  - Lower CD4 cell counts
  - Higher viral loads
- Although risk factors known, impossible to predict which infants will be infected

Perinatal Transmission of HIV

- Pre 1994: USA /Europe: ~ 25% (no Antiretrovirals)
- 1994: Results of 076 study changed practices (AZT) recommendation during pregnancy
- 1995: down to 11% after implementation
- Today, risk of MTCT can be <2% with
  - Effective multi-drug antiretroviral therapy (HAART or ART)
  - Elective C/S when appropriate
  - Exclusive formula feeding
  - Elimination of premastication

TREATMENT PROGRESS

Newer Treatment regimens:

- Multiclass regimens (at least 3)

Laboratory Advancement:

- Viral Load, Genotype, PK levels

Appropriate use of Antepartum & Intrapartum ART, Cesarean Section

THEMES REMAIN THE SAME

- HIV is preventable. Routes of transmission are known but continued transmission
- Stigma related to HIV: Shame, doubt, denial
- Women have sex for many reasons
  - Especially when they have poor self esteem
- HIV can be a scarlet letter
- No one wants to have HIV
- No one wants to have a baby with HIV

TIMING OF PERINATAL TRANSMISSION

Antepartum:

- Greater risk if acute infection occurs during pregnancy
- Initiation of ART as soon as possible (August 2015 Perinatal Guidelines)
- Change regimen as needed (after baseline geno results)

Intrapartum: Majority of transmission is intrapartum

Postpartum:

- Breast feeding, Premastication

ANTEPARTUM CARE:

- Verification of infection
- Baseline labs
- Disclosure counseling
- Discussion of PMTCT
- Treatment options discussed
- Provider-Patient collaborative effort
- Defined goals
- Pregnancy is an incentive: Carrot

BASELINE LABS

- CD4/CD8 ratio
- HIV RNA PCR (Viral Load)
- HIV genotype
  - Interpret results with caution, wild-type, archived mutations
  - Acquired resistant virus, prescribing patterns
- CBC with Diff, platelets
- CMP
- Hepatitis A, B, C assessment
- Renal assessment (Proper calculation of Creatinine Clearance)
- Varicella IgG
- CMV IgM, IgG, Toxo IgM, IgG
- HLA-B 5701 (hypersensitivity to Abacavir, 6-9% in Caucasians)

CHOICE OF ANTIRETROVIRAL TREATMENT

- Durability of Regimen
- Tolerability of Regimen
- Simplicity of Regimen

- Remember your first shot should be a long-lasting option
- Ensure adherence
- Sequencing plan (genotypic profiles)
- Ensure future treatment options (don't blow a whole class)

WHEN DO I START IT?

- Initiation will vary
- Consider teratogenicity
- Consider patient's acceptance of diagnosis, willingness to begin
- Assess nausea, vomiting, food availability
- Start earlier in women with very low CD4 counts
- When is too late to start?
  - Is it ever too late? Depends on who you ask
  - Complete viral suppression will take weeks
  - May be candidate for initiation intrapartum

INITIATION OF HIV TREATMENT IN ART **NAÏVE** PATIENTS

- NIH Guidelines
- Guidelines vs Laws: Read, consult when necessary
- Juxtaposition:
  - Adult Treatment Guidelines vs Perinatal Treatment Guidelines
- Information can be easily accessed (aidsinfo.org)
- Guidelines are frequently updated
- Tables are your friends
- Know pregnancy category, interactions with concomitant medications
- Know your patient's other risk factors

WHAT DO I START THEM ON?

- Multiple factors
  - Comorbidities
    - (lipid friendly, glucose friendly, renal impairment)
  - Convenience
  - Patient adherence potential
  - Adverse effects, education
  - Drug interactions
  - Resistance testing results, PK data, experience in pregnancy
  - Food requirements
  - Gestational age

WHAT DO I START THEM ON?

- Menu of options
- Use appropriate combinations
  - just because drugs are available, does not make them the best choice
    - (Consult most up to date guidelines)
  - Can this patient be successful on this regimen?
  - Remember: lifelong treatment
- In General: Use the same regimens recommended for treatment of non-pregnant adults

WHAT DO I START THEM ON?

- Preferred Regimens: Backbone *Plus*

- Backbone: 2 NRTI combo
  - AZT/3TC (Combivir) FDC, Most experience, twice daily dosing, anemia, Pregnancy Category C
  - TNF/ FTC aka emtricitabine (Truvada) FDC, once daily dosing, TNF careful renal impairment, Pregnancy Category B
  - TNF/ 3TC, once/daily, TNF careful renal impairment, Pregnancy Category C
  - ABC/3TC (Epzicom) FDC, can be once/daily, HSR warning, Must be HLA-B5701 negative, Pregnancy Category C

- Preferred Regimens: Backbone *Plus*

- Plus PI (Protease Inhibitor): More pills, Potent Regimen
  - Darunavir with a Norvir boost (Pregnancy category C)
    - Caution with pts with PI mutations
    - Less experience than Kaletra
    - Once daily dosing not recommended

  - Atazanavir with a Norvir boost (Pregnancy Category B)
    - 2 separate pills when once daily at 300/100
    - increase to 400/100 once daily during 2nd/3rd trimester= 3 separate pills
    - Warn patients about SE, jaundice
    - Lipid friendly option

WHAT DO I START THEM ON?

- Preferred Regimens: Backbone *Plus*

- Plus NNRTI:
  - EFV: What in the world? Pregnancy Category D
  - After 8 weeks gestation, defects in primates only, humans?
  - Truvada/Efavirenz= Atripla FDC one pill, once daily
  - Education re: side effects, caution with pts with h/o mental health issues

WHAT DO I START THEM ON?

- Preferred Regimens: Backbone *Plus*

- Integrase Inhibitor
  - Raltegravir (Pregnancy Category C)
    - 400mg twice/daily
    - Well tolerated

WHAT DO I START THEM ON?

- ***Alternative* Regimens: Backbone *Plus***
- *Plus* PI (Protease Inhibitor): More pills, Potent Regimen
- Lopinavir with a Norvir boost (Pregnancy Category C)
  - Kaletra, FDC
  - Two pills twice daily, increase to 3 pills twice daily during 2nd/3rd trimester
  - Problems with tolerability (GI), pill size, smell

WHAT DO I START THEM ON?

- ***Alternative* Regimens: Backbone *Plus***

- Plus NNRTI (Nevirapine/Viramune):
  - Use only in women with baseline CD4 > 250
  - Pregnancy Category B
  - Risk for hypersensitivity reaction
  - Use caution when using NVP with ABC= Both have risk of HSR
  - Lead in dose (200mg/daily) x 14 d
  - Bring pt back in 14 days to check LFTs before increasing dose (200mg/twice daily), initial prescription: #14?

WHAT DO I START THEM ON?

- Newer options of one pill/once daily regimen
  - FDC Just ONE PILL, ONCE A DAY?
- Approved for Adults
- Insufficient Data to recommend in Pregnancy
  - Limited pharmacokinetic data
  - Limited safety data
- Oh Nooooo!
  - “Sexy” Caution

WHAT DO I START THEM ON?

- ***Insufficient Data*: Backbone *Plus***

- Complera: (FDC Rilpivirine (25mg) + Truvada 200/300)
- Pregnancy Category B
- RPV not recommended with pretreatment HIV RNA >100,000 copies/mL or CD4 cell count < 200, not as forgiving with missed doses
- Caution in Hep B co-infection
- Do not use with PPI
- Limited data in pregnancy

WHAT DO I START THEM ON?

- ***Insufficient Data*: Backbone *Plus***

- Stribild (FDC, cobicistat, elvitegravir, emtricitabine and tenofovir)
- Pregnancy Category B
- Naïve patients, or switch patients that have been fully suppressed on a regimen > 6 months
- Risk of lactic acidosis, more common in women, overweight pts, and pts with liver disease
- Food requirement
- No antacids 2 hr before or after dosing

INITIATION OF HIV TREATMENT IN ART **EXPERIENCED** PATIENTS

- NIH Guidelines
- Guidelines vs Laws: Read, consult when necessary
- Information can be easily accessed (aidsinfo.org)
- Guidelines are frequently updated
- Tables are your friends
- Know pregnancy category, interactions with concomitant medications
- Know your patient's other risk factors
- Start an investigation

INITIATION OF HIV TREATMENT IN ART **EXPERIENCED** PATIENTS

- Investigation (really)
- Time Consuming
- Medical records + patient report
- Date of diagnosis
- Initial CD4, VL, genotype
- Initial regimen (start and stop date, why changed? genotype)
- Next regimen (start and stop date, why changed? genotype)
- Serial genotypes help you determine potential mutations, archived mutations that you will not see in genotype without drug pressure

THEN WHAT DO I DO?

- Follow-up labs for toxicity

- Toxicity:
  - Depends on the drugs prescribed
  - 2 week after initiation of ART
  - CBCD
    - (AZT related anemia),
  - CMP
    - (NNRTI hepatatoxicity, PI hepatatoxicity, Tenofovir related renal impairment)

THEN WHAT DO I DO?

- Follow up labs for immune reconstitution

- CD4 Changes:
  - Varies: 3 months after initiation of ART
  - then every 3 months in pregnancy
  - every 6 months in non-pregnant patients with ARV regimen-related immune reconstitution)
  - consider more frequent monitoring if CD4 is around threshold for OI prophylaxis (CD4 Absolute ~200)

THEN WHAT DO I DO?

- **Follow-up labs for Virologic response, Resistance, "Extra"**

- Virologic Response: HIV RNA PCR (HIV Viral Load):
  - 2-4 wks after initiation (varies according to gestational age, baseline labs),
  - then monthly until undetectable.
  - What if the response is too slow or isn't moving toward undetectable?
    - (should be undetectable in approx. 12 weeks)
  - Remember: Any detectable virus is causing some damage, somewhere
  - Repeat between 34 and 36 weeks for delivery plan

THEN WHAT DO I DO?

- **Follow-up labs for Resistance, "Extra"**
- Genotypic testing:
  - remember: you need detectable virus to complete the test (500 -1000 copies)
  - Baseline, Repeat when there is suboptimal suppression on ART
- Glucose testing:
  - May want to complete prior to 24 week sample in women on a prolonged protease inhibitor containing regimen that was initiated prior to pregnancy
  - 24-28 week

THEN WHAT DO I DO?

- Need an Amnio?
  - Former strict contraindication
  - No perinatal transmissions have been reported after amnio in women with full virologic suppression on ART
  - Small risk of transmission cannot be ruled out on successful ART regimen
  - Risk/benefit when viral load is undetectable, pt is on ART, consult with expert
  - Caution

ADDITIONAL CONSIDERATIONS

- Education
- Support: Similar goals: Maintaining maternal health, preventing MTCT
- Disclosure counseling, partner education
- Safe sex counseling (discordant, concordant couples)
- Early ultrasound for determination of gestational age
  - Teratogenicity risk?
  - Dating for possible elective Cesarean Section

PREGNANCY IN HIV+ WOMEN
HIGH-RISK PREGNANCY?

- Physiologic changes during pregnancy
  - Drug absorption, distribution, possible need for increased dosing during second and third trimesters
  - Complications of Pregnancy, potentially altering susceptibility of pregnant women to drug toxicity
  - Placental transport of drugs, biotransformation of drugs by fetus and placenta
  - Know pharmacokinetic dosing recommendations
  - Immunosuppression R/T pregnancy

INTRAPARTUM CARE

- Mode of Delivery
- Make a plan, realize they change
- Elective Cesarean Section 38 weeks
  - Before ROM
  - Before onset of labor
  - Statistical benefit if the horse is out of the barn?
    - Plan individualized: Duration of ROM, Current ARV regimen, VL
  - Last Viral Load > 1000 copies, unknown VL
  - L/D New Diagnoses

INTRAPARTUM CARE

- Antiretroviral dosing
- Continue antepartum PO regimen during labor (NPO?)
- Use of IV AZT/ZDV: guidelines changed 3-28-2014
- Continues in patients with VL > 1000 copies
  - Ideal: loading dose 1mg/kg over an hr, maintenance 2mg/kg/hr
  - Duration: at least 3 hr total
  - Please weigh pt on admission
- Maternal or Fetal Indications: Use judgement, Load only?
- Rupture < 37 weeks: Steroids, delivery plan based on best obstetrical practices
- Amnio NOT recommended for fetal lung maturity

INTRAPARTUM CARE

- MTCT has occurred with very low levels of detectable virus (VL<1000)
- European Collaborative Study:
  - Cesarean Delivery in VL <50 or <200 was associated with reduction of perinatal transmission
  - After adjustment for ARV use (none vs any), effect was no longer significant
- Benefit of scheduled cesarean delivery? Difficult decision, discuss pro/con; risk/benefit
- Talk to your patient, tell them what you know, statistics you have
- You can never guarantee that a baby will not be HIV-positive

INTRAPARTUM CARE

- Risk of maternal complications
- Research has shown that HIV+ women have increased rates of postoperative complications, mostly infectious.
- Related to degree of immunosuppression and receipt of ART

- Urgent cesarean delivery: highest risk of pp morbidity
- Scheduled cesarean delivery: intermediate risk of pp morbidity
- Vaginal delivery: lowest risk of pp morbidity

POSTPARTUM PLAN FOR MOM

- 2 week pp visit
- Vaginal and cesarean section
- Baby feeding? Bottle? Giving ARV to baby? Taking your ARV?
- Screen for pp depression
- Inquire about support
- Disclosure?
- What about giving baby meds in front of others? Breastfeeding in front of others?
- Infant f/u appointment

POSTPARTUM PLAN FOR MOM

- Continuation of ARV?
- Remember it is better to discontinue all ARV than to be nonadherent, even for short periods of time
- Plan for Infectious Disease follow-up, help them make appt
- (NKS- baby is out, carrot is gone, HIV does not hurt, denial)
- PP birth control
- Future pregnancy planning
- Safe sex counseling

POSTPARTUM EDUCATION FOR INFANT CARE

- Breastfeeding vs formula feeding (exclusive)
- Act of premastication (Gaur, Pediatrics, Aug 2009)
- Infant ARV treatment
- Follow-up with peds ID
  - 1st visit~ 2 weeks of age
  - Proper testing
  - Weight-based changes for dosing of ARV
  - Serial testing= can actually time the point of transmission

DESPITE ALL OF THE RESEARCH AND KNOWLEDGE

- There are still approximately 200 perinatal infections each year in the US

- How?
  - Lack of HIV testing
  - Lack of prenatal care
  - Sub-optimal HIV management
  - Adherence to regimen? Maternal? Infant?

REFERENCE

- aidsinfo.org (Perinatal Guidelines)