HIV and conception

Fiona Lyons, MD
GUIDE Clinic, St. James’s Hospital, Dublin, Ireland
Dublin

www.guideclinic.ie
Adults and children estimated to be living with HIV | 2012

Total: 35.3 million [32.2 million – 38.8 million]

What to consider?

• What are our patients thinking?
• Safe conception
  – Other than HIV issues…periconceptual FA, ETOH and cigarette smoking
  – Risk of onward HIV transmission
    • Vertical and horizontal
  – Risk of teratogenicity and toxicity
    • HIV
    • ARVs
  – Co-morbidities
What to consider?

• What are the chances of conception?

• If chances of conception are suboptimal – what are the choices?
  – IUI
  – IVF
  – ICSI
What are our patients thinking?
What are our patients thinking?

• When we see patients do they know the “correct” answer to give?
  – “No” I’m not having sex
  – “Yes” my partner knows I am HIV positive
  – “No” I don’t practice “unsafe” sex
Planned or unplanned?

Unplanned Pregnancies among HIV-infected Women in Care - United States.  
*Sutton MY, et al*

- 382 pregnancies reported 85% unplanned

High prevalence of unintended pregnancies in HIV-positive women of reproductive age in Ontario, Canada: a retrospective study.  
*Loutfy M, et al*

- 56% of last pregnancies unplanned

Pregnancy in HIV-infected teenagers in London.  
*Elgalib A, et al*

- 85% pregnancies unplanned (many diagnosed antenatally), with 12 months 25% pregnant again
What are our patients thinking?

• We need to ask our patients what they are thinking when it comes to parenthood
  – Facilitate planned and avoid unplanned pregnancies
  – Desire for parenthood in people living with HIV
What are our patients thinking?

- Surely I can’t have children
- Will I survive to see my children grow up?
- What is the risk that I will infect my partner?
- Will pregnancy make my HIV worse?
- What is the risk of my baby being infected?
- Could HIV make my baby abnormal?
- Will the treatment harm my baby?
- Will the treatment harm me?
Safe Conception

- Preventing horizontal and vertical transmission
- Avoiding teratogenicity and ART toxicity
- Managing co-morbidities
Seroconcordant couples: safe reproductive options

HIV+ male and HIV+ female

- Adoption
- Optimisation of HIV and co-morbidities
- Assessment for and treatment of STIs
- Education about menstrual cycle and fertile period
- Assessment of fertility and referral for assisted reproductive technologies
Serodiscordant couples: safe reproductive options

HIV+ female and HIV- male

- Adoption
- Insemination with partners sperm at ovulation
- Natural conception (if effective viral suppression) +/- PrEP-C
- Assisted reproduction (if fertility issues)

*PrEP-C = use of ARVs by negative partner for prevention of HIV transmission around conception
Serodiscordant couples: safe reproductive options

HIV+ male and HIV- female

• Adoption
• Donor insemination
• Sperm washing +/- IUI, IVF, ICSI
• “Natural” conception
  – Timed intercourse
  – ART for positive partner
  – STI treatment
  – Use of PrEP-C*

*PrEP-C = use of ARVs by negative partner for prevention of HIV transmission around conception
Position statement on the use of antiretroviral therapy to reduce HIV transmission January 2013. The British HIV Association (BHIVA) and the Expert Advisory Group on AIDS (EAGA)†

†Members of the Writing Group: S Fidler¹, J Anderson², Y Azad³, V Delpech⁴, C Evans⁵, M Fisher⁶, B Gazzard⁵, N Gill⁴, L Lazarus⁴, R Lowbury⁷, K Orton⁸, B Osoro⁹, K Radcliffe¹⁰, B Smith¹¹, D Churchill⁶, K Rogstad¹² and G Cairns¹³

GUIDANCE ON COUPLES HIV TESTING AND COUNSELLING INCLUDING ANTIRETROVIRAL THERAPY FOR TREATMENT AND PREVENTION IN SERODISCORDANT COUPLES

Recommendations for a public health approach

April 2012

ART also is recommended for HIV-infected individuals for the prevention of transmission of HIV. The strength and evidence for this recommendation vary by transmission risks: perinatal transmission (AI); heterosexual transmission (AI); other transmission risk groups (AIII).
Sperm washing

- HIV cannot attach to or infect spermatozoa due to lack of receptors
- Centrifugation of ‘sperm’ performed in specialist units to remove HIV
Sperm washing

- Sperm washing can be used in conjunction with assisted reproductive technologies – such as IUI, IVF, ICSI +/- ovulation induction – if additional fertility issues
- Observational studies demonstrating safety and efficacy of sperm washing\textsuperscript{1, 2, 3}
  - 14% live birth rate per treatment cycle using intrauterine insemination (IUI)
  - 35% live birth rate for IVF or ICSI
  - No HIV transmissions

\textsuperscript{1}Bujan L et al. AIDS 2007 \textsuperscript{2}Garrido N et al. Hum Reprod 2004 \textsuperscript{3}Nicopoullos JD et al. Hum Fertil 2010
Why not sperm washing?

- Expensive
  - Ineligible for public funding
  - Unable to afford privately
- Lack of widespread availability
- Inconvenient
- ‘Failure’ (up to 30% drop out before starting insemination; 30% do not complete)
- Increasing requests for ‘natural’ conception
HIV-1 transmission

• Depends on
  – HIV plasma viral load
  – Type of exposure to HIV
  – Presence of sexually transmitted infections
The evidence

- Prevention of MTCT
- Observational studies in serodiscordant couples
- Randomised controlled trial
Stable, healthy, serodiscordant couples, sexually active
CD4 count: 350 to 550 cells/mm³

Primary Transmission Endpoint
Virologically-linked transmission events

Primary Clinical Endpoint
WHO stage 4 clinical events, pulmonary tuberculosis, severe bacterial infection and/or death

Cohen MS et al. NEJM 2011; 365: 493-505
Total HIV-1 Transmission Events: 39

Linked Transmissions: 28
Unlinked or TBD Transmissions: 11

Early ART led to a 96% reduction of sexual transmission of HIV-1 in serodiscordant couples

Immediate Arm: 1
Delayed Arm: 27

Single transmission in patient in immediate HAART arm believed to have occurred close to time therapy began and prior to suppression of genital tract HIV

\[ p < 0.001 \]
PrEPc
Safety of PrEP-C

• Use of tenofovir/truvada in HIV negative individuals as PEP(SE)
• PrEP trials
• Use of tenofovir/truvada in HIV positive pregnant women and infants born to these mothers
• Recent data from IAS 2013
PrEP-C
Vernazza P.L. et al. AIDS 2011; 25

Pregnancy rate per menstrual cycle
Abstract

WEAC0101 - Oral Abstract Session

Pregnancy incidence and birth outcomes among African women in a clinical trial of pre-exposure prophylaxis: the Partners PrEP Study

Presented by Elizabeth Bukusi (Kenya).

N. Mugo1,2, T. Hong2, C. Celum2, D. Donnell3, E. Bukusi4, E. Were5, G. John-Stewart6, J. Baeten2, Partners PrEP Study

1Kenya Medical Research Center, Center for Clinical Research, Nairobi, Kenya, 2University of Washington, Global Health, International Center for Clinical Research, Seattle, United States, 3Fred Hutchinson Cancer Research Center, Seattle, United States, 4Kenya Medical Research Institute, Nairobi, Kenya, 5Mo University, Obstetrics and Gynaecology, Eldoret, Kenya, 6University of Washington, Global Health, Seattle, United States

Background: Antiretroviral pre-exposure prophylaxis (PrEP), using daily oral tenofovir disoproxyl fumarate (TDF) and combination emtricitabine (FTC)/TDF, is highly efficacious for prevention of HIV acquisition. Implementation of PrEP for HIV prevention will require data on its safety in women who become pregnant.

Methods: We conducted a randomized, three-arm trial of oral PrEP among HIV serodiscordant heterosexual couples from Kenya and Uganda (the Partners PrEP Study), including 1785 couples with HIV uninfected female partners. Seronegative partners were randomized to TDF, FTC/TDF, or placebo and followed monthly for 24-36 months, including monthly HIV and pregnancy testing. HIV uninfected women were not pregnant at the time of study enrollment; if they became pregnant, the study medication was discontinued for the duration of pregnancy and lactation. Infants born to HIV uninfected women were followed at quarterly visits for 12 months after birth. In July 2011, the study placebo arm was discontinued, due to demonstration of PrEP efficacy for HIV prevention. We present updated data on pregnancies conceived as of July 2011.

Results: A total of 288 pregnancies occurred among 267 women, with similar incidence rates across the trial randomization study arms: TDF 11.9 per 100 person-years (p=0.19 vs. placebo), FTC/TDF 8.8 (p=0.40 vs. placebo), placebo 10.0. Of the 288 pregnancies, 192 (66.7%) ended in live births and 96 (33.3%) ended in pregnancy losses, most (91.7%) occurred at < 20 weeks of gestation; pregnancy outcomes did not differ statistically across the study arms. Median birth weight was similar across the study arms: TDF 3368 gm (p=0.54 vs. placebo), FTC/TDF 3352 gm (p=0.68 vs. placebo), placebo 3290 gm. Infants born to women randomized to PrEP versus placebo had similar WHO gestational age-adjusted Z-scores for head circumference, length, and weight throughout the first year of life.

Conclusion: In this randomized, placebo-controlled trial of PrEP, pregnancy incidence, losses, outcomes, and infant growth were similar for women receiving PrEP and placebo at the time of conception. PrEP may offer a method for HIV uninfected women with HIV infected partners to reduce risk of infection during conception.
Benefits of PrEP as an adjunctive method of HIV prevention during attempted conception between HIV-uninfected women and HIV-infected male partners: A modeling approach

R. Hoffman¹, R. Vardavas², A. Jaycocks², G. Wagner², J. Lake¹, D. Mindry³, J. Currier¹, R. Landovitz¹
Average Probability of Female Remaining HIV-1-uninfected with Child

- **optimal**
- **suboptimal**

<table>
<thead>
<tr>
<th>Scenario</th>
<th>Annual Probability</th>
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<tbody>
<tr>
<td>No Treatment or PrEP</td>
<td>29.5%</td>
</tr>
<tr>
<td>PrEP</td>
<td>31.3%†</td>
</tr>
<tr>
<td>Treatment</td>
<td>33.3%*</td>
</tr>
<tr>
<td>Treatment + PrEP</td>
<td>33.5%*</td>
</tr>
<tr>
<td></td>
<td>32.6%†</td>
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- one standard deviation above and below the mean
- * statistically different at the 0.001 level from the ‘No Treatment or PrEP’ option
- † statistically different at the 0.001 level from both the ‘No Treatment or PrEP’ and ‘Treatment’ options

Treatment = ART for the HIV-1-infected male
PrEP = Pre-exposure prophylaxis for the HIV-1-uninfected female
p-values calculated using t-tests comparing means in optimal scenarios and separately comparing means in suboptimal scenarios
Our approach at GUIDE

- **Advice on options**
  - Adoption, donor insemination
  - Sperm washing
  - UPSI...
  - Timed UPSI (assessment of fertility)
  - PrEP-C

- **Clear understanding of risks and *mutual* consent**
  - We always see together and separately

- **Diagnose and treat STIs**

- **Try to make it more normal and less like a military operation!**
Safe Conception

☑ Preventing horizontal and vertical transmission

☑ Avoiding teratogenicity and ART toxicity

☑ Managing co-morbidities
Antiretroviral pregnancy Registry
1st Jan 89 – end July 2013

- 15451 live births exposure at any time
- Overall birth defects (/100 live births) 2.9
- CDC population based survey 2.72
- First trimester 2.9
- 2nd and 3rd trimester 2.8

Available at www.apregistry.com
What are the chances of conception?
Female fertility and HIV

• Nature knows best
  – Weight
  – Nutritional status
  – Opportunistic infections
• Earlier menopause
Male fertility and HIV

- Impact of HIV on semen quality
- Impact of ARVs on semen quality
What if the chances are suboptimal?

• Access to assisted reproductive technologies
  – IUI, IVF and ICSI

• Where I work no access to IVF or ICSI
  – Couples travel to the UK or mainland Europe
  – Work closely with units to facilitate as much as possible
Conception and HIV

• We need to consider patients wishes around conception
  – Male and female patients
  – Patients have learned the “correct” answers in clinics – *personal observation!*
  – We should ask the questions

• Significant proportion of pregnancies are unplanned

• Many patients desire parenthood

• Options vary hugely