Hormonal contraception and HIV disease progression: a multi-country analysis of the MTCT Plus cohort

Hormonal Contraception and HIV

- 15 million women HIV-infected
  - Most need contraception
- Hormonal contraception widely used worldwide
- Some studies suggest HC may accelerate HIV
  - Mombasa, Kenya
  - RCT in Zambia
Time to disease progression by randomization arm (IUD RCT)

Log Rank P-Value : 0.012

At Risk
IUD 296 271 258 192 111 37
Hormonal 303 269 245 150 86 37

Proportion Dying or Falling Below 200

IUD
Hormonal
Hypothesis

Hormonal Contraception (HC) hastens HIV disease progression
The MTCT-Plus Initiative

- Pregnant and newly postpartum HIV-infected mother entry point into care
- 7,846 women enrolled and followed between 2003 – 2008
- CD4⁺ counts q 6 mo
- Contraceptive use based on women’s self-report
- Condoms provided and encouraged
- Family planning methods varied by site
Methods: Eligibility criteria for analysis

- ART-naive at time of enrollment
- Not pregnant or within 90 days of delivery
- Available contraception data
- Available CD4+ data at enrollment
Methods: Defining exposure

**Progesterone-only exposure**
- Implants (Norplant, Jadelle)
- Injectables (DMPA, Lunelle)

**Combined estrogen-progesterone**
- Oral contraceptive pills (OCPs)

**No exposure to exogenous hormones**
- No contraception
- All non-hormonal methods (condoms, rhythm method, IUD, LAM)
Primary Outcome

• Disease progression defined as:
  – Becoming eligible for ART
    • CD4+ cell count falling below 200 cells
    • WHO Stage IV
    • WHO Stage III with CD4 cell count < 350 cells
  – Death
Analysis

• Data obtained from standardized forms completed at each visit
• Time-to-disease progression estimated with Kaplan Meier method and Cox proportional hazards regression
• Contraceptive exposure was categorized as
  – Initial method
  – Time-varying
MTCT Plus Cohort Profile

Women Enrolled (N=7846)

Analysis Eligible (N=4530)

- Non-HC (N=3099)
- Injectables/Implants (N=830)
- OCPs (N=226)

Not Eligible (N=3316)

Unknown (N=375)
## Baseline Characteristics

<table>
<thead>
<tr>
<th></th>
<th>Non hormonal</th>
<th>Progest Only</th>
<th>P value</th>
<th>Combined E/P</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median yrs, (IQR)</td>
<td>27 (24,31)</td>
<td>27 (24,30)</td>
<td>&lt;0.01</td>
<td>28 (24,32)</td>
<td>0.26</td>
</tr>
<tr>
<td>Parity, median (IQR)</td>
<td>2 (1,3)</td>
<td>2 (1,3)</td>
<td>0.65</td>
<td>2 (1,3)</td>
<td>0.12</td>
</tr>
<tr>
<td>Widowed (%)</td>
<td>5.0%</td>
<td>1.0%</td>
<td>0.23</td>
<td>1.8%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>23 (21,26)</td>
<td>24 (22, 28)</td>
<td>&lt;0.01</td>
<td>24 (21, 26)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>CD4+ cell count</td>
<td>31, 627</td>
<td>34, 618</td>
<td>0.25</td>
<td>34, 605</td>
<td>0.43</td>
</tr>
<tr>
<td>Hb</td>
<td>12 (10, 13)</td>
<td>12 (11, 13)</td>
<td>&lt;0.01</td>
<td>12 (11, 13)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Condom usage (%)</td>
<td>36.4%</td>
<td>29.6%</td>
<td>&lt;0.01</td>
<td>20.4%</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>
## Results

<table>
<thead>
<tr>
<th></th>
<th>Events</th>
<th>Rate*</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death</td>
<td>66</td>
<td>1.1</td>
<td>0.9 – 1.4</td>
</tr>
<tr>
<td>ART eligible</td>
<td>881</td>
<td>17.0</td>
<td>15.9 – 18.2</td>
</tr>
<tr>
<td>Death or eligible</td>
<td>902</td>
<td>17.4</td>
<td>16.3 – 18.6</td>
</tr>
</tbody>
</table>

*Rate per 100 woman-years
Time to primary outcome, by initial exposure

- No hormonal exposure
- Progesterone-only exposure
- Combined estrogen-progesterone exposure

Log Rank P-Value: 0.42
## Results: Primary Outcome

<table>
<thead>
<tr>
<th></th>
<th>Initial Method</th>
<th>Time-Varying</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>HR (95% CI)</td>
<td>AHR (95% CI)</td>
</tr>
<tr>
<td>No exposure</td>
<td>1.0</td>
<td>1.0</td>
</tr>
<tr>
<td>Progesterone-only</td>
<td>1.0 (0.8-1.2)</td>
<td>1.0 (0.8-1.2)</td>
</tr>
<tr>
<td>Combined estrogen-progesterone</td>
<td>1.0 (0.7-1.3)</td>
<td>0.9 (0.6-1.2)</td>
</tr>
</tbody>
</table>

*Controlling for age, parity, baseline WHO Stage, CD4 count, BMI, Hb, condom usage, site*
Hazard of disease progression by site

- Overall
- Cameroon
- Mozambique
- Langa/Cape Town
- Mulago (Uganda)
- Eldoret (Kenya)
- Rwanda
- Cato Manor (S.A.)
- Soweto (S.A.)
- Zambia
- Nsyamba (Uganda)
- Thailand
- Kisumu (Kenya)
- Cote D'Ivoire

HR (95% CI)
Hazard of disease progression by site (OCPs)
Strengths and limitations

• Strengths
  – Large, multi-country cohort
  – Diversity of patients, viral sub-types, and contraceptive methods

• Limitations
  – Accurate categorization of contraceptive exposure
  – Observational data; potential for self-selection
Conclusions

• No evidence of hormonal contraception accelerating HIV disease progression in this dataset
• Differences between progesterone-based methods of contraception could not be elucidated
• Further research in this field is urgently needed
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  - Langa Clinic, City of Cape Town Health Dept, Cape Town, South Africa
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  - Chelstone and Mtendere District Health Clinics, Lusaka, Zambia

- MTCT Plus patients
- Lusaka District Health Board
- Chibesa Wamalume
End