Contraception in HIV-positive women

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GLOBAL STATISTICS

- 36.9 million [34.3 million–41.4 million] people globally were living with HIV (end 2014)
- 15.8 million people accessing antiretroviral therapy (June 2015)
- 2 million [1.9 million–2.2 million] people became newly infected with HIV (end 2014)
- 2 million [980 000–1.6 million] people died from AIDS-related illnesses (end 2014)
- The Joint United Nations Programme on HIV/AIDS (UNAIDS) and WHO – the main organizations collecting HIV infection epidemiological data and providing recommendations

UNAIDS data, 2014

New HIV diagnoses per 100 000 population, 2014

New HIV diagnoses per 100 000 population, 2014

- Estonia 22.1 new cases / 100 000 population
- Latvia 17.3 new cases / 100 000 population
- Luxembourg 12.6 new cases / 100 000 population
- Lithuania 4.8 new cases / 100 000 population
- Croatia 2.2 new cases / 100 000 population
- Czech Republic 2.2 new cases / 100 000 population
- Slovakia 1.6 new cases / 100 000 population

New HIV cases in Lithuania till 2009

- Estonia
- Latvia
- Luxembourg
- Lithuania
- Croatia
- Czech Republic
- Slovakia
Percentage of new HIV diagnoses with known mode of transmission, by transmission route and country, EU/EEA, 2014 (n=24 083)

Pregnancies in women living with HIV

• While three million women living with HIV (WLWH) give birth each year (UNAIDS, 2010), the clinical guidance on reproductive health in this group has concentrated primarily on the health of the unborn baby and the prevention of mother-to-child transmission (MTCT) rather than on the expectant mother’s health

Concerns Regarding Contraception in the HIV-positive Patient (1)

• Majority of women living with HIV (WLWH) are of reproductive age, so, family planning is a very important aspect of their life. Several studies reported that pregnancies in this population are unintended in 50-83% of cases (Floridia et al., 2006; Koenig, Espinosa, Hodge, & Ruffo, 2007; Loutfy et al., 2012a).
• Tailored reproductive counseling and contraception discussions early in the course of HIV care are crucial for all women to prevent unintended pregnancies.

Concerns Regarding Contraception in the HIV-positive Patient (2)

• Need for reliable and efficacious birth control in women on potentially teratogenic drugs (Tseng A, Hills-Nieminen C, 2013).
• Another fundamental consideration is reversibility and the option for future pregnancy. Cross-sectional data from Brazil suggest that 40% of HIV-positive women had a desire for future pregnancy, while data from Ontario showed that 50% of HIV-positive women wanted to speak to an obstetrician about pregnancy planning (da Silva Rossi A et al., 2005, Zhang Y et al., 2012).
• Cost, cultural factors, acceptability, availability, and need for partner participation are also important considerations.

Efficacy in Pregnancy Prevention

• User-independent methods such as the intrauterine device [with or without levonorgestrel] are > 99% effective.
• Injectable methods are 99.7% effective when used perfectly, and 97% effective with typical use.
• Most hormonal methods are over 99% effective with perfect use, but efficacy drops to 95% with more typical usage.
• Other non-user-dependent methods have efficacy rates closer to 85% with typical use.
• There are no comparative or cohort studies on the efficacy of various contraceptive modalities in HIV infection. However, the efficacy of hormonal contraceptives can be influenced by concomitant use of ART or antituberculous medications (Tsang A, Hills-Nieminen C, 2013; Zhang Y et al, 2011).

Dual contraception in WLWH

• Since condoms are poor at preventing pregnancy, but required to prevent HIV and STIs, dual protection including a hormonal contraceptive (or copper intrauterine device) and a condom is recommended (Department of Health and Human Services, 2011; WHO, 2012).
Advantages and disadvantages of contraception options in HIV.

### Condoms (Trussell, 2007)

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Condom (male)</td>
<td>STI/HIV protection</td>
<td>Requires correct technique</td>
</tr>
<tr>
<td></td>
<td></td>
<td>May interfere with intercourse</td>
</tr>
<tr>
<td>Condom (female)</td>
<td>STI/HIV protection</td>
<td>May interfere with intercourse</td>
</tr>
<tr>
<td></td>
<td>May be controlled by woman</td>
<td>Pregnancy prevention 85%</td>
</tr>
</tbody>
</table>

**Advantages:**
- Effective
- Low blood loss
- Can be controlled by woman
- Pregnancy prevention 92%

**Disadvantages:**
- Requires correct technique
- May interfere with intercourse
- Pregnancy prevention 85%
- No STI/HIV protection

**HIV transmission: spermicides use**

- There are several important ways in which contraceptive methods can impact the transmission of HIV. Spermicides, which are often used with diaphragms or cervical caps, can cause epithelial irritation and ulceration, which may facilitate STI and HIV transmission (Kreiss et al., 1992).

**Advantages and disadvantages of contraception options in HIV. Hormonal contraception (Trussell, 2007)**

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Oral contraceptive pills</td>
<td>Effective</td>
<td>Drug-drug interactions</td>
</tr>
<tr>
<td></td>
<td>less blood loss</td>
<td>Possible viricide shedding</td>
</tr>
<tr>
<td></td>
<td>Can be controlled by woman</td>
<td>Increased viral shedding</td>
</tr>
<tr>
<td></td>
<td>Pregnancy prevention 89%</td>
<td>No STI/HIV protection</td>
</tr>
<tr>
<td>Patch, ring, injectable</td>
<td>Effective</td>
<td>Drug-drug interactions</td>
</tr>
<tr>
<td>combination</td>
<td>less blood loss</td>
<td>Increased viricide shedding</td>
</tr>
<tr>
<td></td>
<td>Can be controlled by woman</td>
<td>No STI/HIV protection</td>
</tr>
<tr>
<td></td>
<td>Pregnancy prevention 89%</td>
<td></td>
</tr>
<tr>
<td>DMPA</td>
<td>Low maintenance</td>
<td>Drug-drug interactions</td>
</tr>
<tr>
<td></td>
<td>Can be controlled by woman</td>
<td>Possible viricide shedding</td>
</tr>
<tr>
<td></td>
<td>Pregnancy prevention 92%</td>
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</tr>
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</table>

**Progression of HIV in relation to hormonal contraception: systematic reviews data**

- A 2009 systematic review looking at progression, health outcomes and transmission of HIV to negative partners found one study with no association between contraception and viral shedding, and nine others with inconsistent results (Curtis KM et al., 2009).
- A 2013 systematic review noted 10 separate cohort studies relating any association between hormonal contraception (OC or DMPA) use and HIV disease progression as measured by viral load set point, HIV RNA levels, CD4 counts, or progression to ART initiation (Philips Sl et al., 2013). Importantly, all studies lacked power calculations!

**Evidence, that progesterone only injectable contraceptive methods increase risk for HIV acquisition or transmission**

- A recent study has reported that women using hormonal contraceptives, specifically depot medroxyprogesterone acetate (DMPA), had twice the risk of acquiring or transmitting HIV as other women (Heffron et al., 2012).
- A sub analysis of the Methods for Improving Reproductive Health in Africa study found that combined oral contraceptive (CC) or progesterone only pill (POP) use was not associated with an increased risk of HIV acquisition (OR: 95% CI 0.63-1.39; PDP: HR 0.84, 95% CI 0.45-1.60), but progesterone only injectable contraceptive methods (DMPA and medroxyprogesterone enantate) were [HR 1.41, 95% CI 1.01-1.91], (McCoy et al., 2012).

**HIV and hormonal contraception (UNAIDS & WHO)**

- WHO has announced in February 2012 that its current recommendation—no restrictions on the use of hormonal contraceptives to avoid unintended pregnancies for women at high risk of, or living with HIV—which is based on current evidence, remains unchanged. In addition, it recommends that women using progesterone only injectable contraceptives also use condoms or other measures to prevent HIV infection.
Advantages and disadvantages of contraception options in HIV.

Intrauterine contraception, sterilisation (Trussell, L. 2007).

<table>
<thead>
<tr>
<th>Method</th>
<th>Advantages</th>
<th>Disadvantages</th>
</tr>
</thead>
<tbody>
<tr>
<td>Copper intrauterine device</td>
<td>Effective</td>
<td>Blood loss</td>
</tr>
<tr>
<td></td>
<td>Conventional</td>
<td>Increased pelvic infection</td>
</tr>
<tr>
<td></td>
<td>Can be controlled by woman</td>
<td>No STI/HIV protection</td>
</tr>
<tr>
<td>Sterilisation</td>
<td>Long lasting</td>
<td>Blood loss</td>
</tr>
<tr>
<td></td>
<td>Effective</td>
<td>No STI/HIV protection</td>
</tr>
<tr>
<td></td>
<td>Prevents pregnancy</td>
<td>Mf only research available in HIV</td>
</tr>
<tr>
<td></td>
<td>Durability</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No hormonal contraception</td>
<td></td>
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<tr>
<td></td>
<td>Irreversible</td>
<td></td>
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<tr>
<td></td>
<td>Depended</td>
<td></td>
</tr>
<tr>
<td></td>
<td>No STI/HIV protection</td>
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</table>

Progression of HIV infection: hormonal contraception vs IUD

- A single randomized controlled trial compared hormonal contraception (DMPr or OC) with copper IUD among HIV-positive women. It demonstrated less HIV disease progression, measured by CD4 count decline to < 200 cells/μL and death in IUD users [relative risk (RR) 0.66; 95% CI 0.46-0.96] (Stringer EM et al., 2007).

Drug interactions

- Hormonal contraceptives are generally metabolized by hepatic cytochrome P450 (CYP450) isoenzymes and hepatic sulfate and glucuronide conjugation. Many components of ART can induce or inhibit the CYP450 system with subsequent potential for clinically significant interactions.
- Protease inhibitors may decrease the concentration and efficacy of hormonal contraception by increasing steroid metabolism and lowered EE levels (El-Halawe MI, Cocolis JM, 2008; Clark RA, Tshul K, 2004).
- Nucleotide reverse transcriptase inhibitors (NRTIs) are newly eliminated with no CYP450 metabolism. They are thus relatively safe to use with most forms of oral contraception (OC) and no specific modifications are necessary (Kreamer BP, Mathias A, 2009).

Drug interactions

- Most nonnucleoside reverse transcriptase inhibitors (NRTIs) induce CYP enzymes — check drug-drug interaction for the ART agent (Kreamer BP, Mathias A, 2009).
- Integrate inhibitors are now a component of recommended first-line ART for the treatment of HIV infection. Some of them lower the effective dose of EE, and thus it is recommended that a minimum of 30 μg of EE be used (German P et al., 2013)
The Ring Study

A study conducted in multiple countries in Sub-Saharan Africa showed that a vaginal ring containing dapivirine can provide some protection against HIV acquisition.

Future research

- For the first time, two trials demonstrated that a female-controlled HIV prevention method can safely help reduce new HIV infections.
- Vaginal rings have the potential to release both an HIV prevention and contraceptive product. In addition, these products can be women-initiated and could therefore empower women in their sexual and reproductive health choices.
- WHO states its commitment to continue to support research and development of innovative prevention products and delivery mechanisms that meet multiple sexual and reproductive health needs of young women living in settings with high incidence of HIV.
Recommendations

- Fertility desires and contraception should be discussed with all HIV-positive women.
- Condoms are key to preventing HIV and STI transmission but suboptimal for pregnancy prevention and other methods need to be considered in combination with barrier protection.
- There are several important drug interactions between hormonal contraceptives and ART.
- Oral and injectable hormonal contraception methods do not appear to be associated with progression of HIV disease.
- Progestogen-containing injectable contraceptive methods may be associated with a slightly reduced risk of HIV transmission and acquisition, which must be considered carefully in high-risk patients.
- Cardiovascular risk factors (especially smoking) should be addressed prior to initiating hormonal contraception.

Conclusions

- In 50-83% of cases in women living with HIV (WLWH) pregnancies are unintended.
- All advantages and disadvantages of available contraceptive options should be evaluated during contraceptive counselling of WLWH and potential interactions with antiretroviral treatment should be taken into the account.
- Dual protection including a hormonal contraceptive (or copper intrauterine device) and a condom is needed for WLWH.
- Further research on contraceptive methods use in WLWH is needed to optimize health care and ensure WLWH rights.

Thank you for your attention and we kindly invite you to vote for ESC Congress 2020 in Vilnius!