Hormonal Contraceptive Use is Associated with Elevated Innate Immune Effector Molecules in Cervicovaginal Secretions of HIV-1-uninfected Women

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BACKGROUND. The injectable hormonal contraceptive depot medroxyprogesterone acetate (DMPA) may increase risk of HIV acquisition. Sex hormones may affect the cationic polypeptides that constitute an important arm of the innate immune response in the cervicovaginal mucosa. We assessed cationic polypeptide levels in relation to DMPA use.

METHODS. HIV-negative women were recruited from among couples testing for HIV in Nairobi, Kenya. Cervicovaginal secretion (CVS) samples were collected and cationic polypeptide concentrations were measured by enzyme-linked immunosorbent assays (ELISA). Levels of cationic polypeptides in CVS were compared between women who were not using hormonal contraception and those using DMPA, oral, or implantable contraception.

RESULTS. Among 228 women, 165 (72%) reported not using hormonal contraception at enrollment, 41 (18%) used DMPA, 16 (7%) used an oral contraceptive, and 6 (3%) used a contraceptive implant. Compared to non-users, DMPA users had significantly higher mean levels of HNP1-3 (2.38 vs. 2.05 log10 ng/ml; p = 0.04) and Lactoferrin (LL-37) (0.39 vs. 0.31 log10 ng/ml; p = 0.02). In the multivariable analysis, DMPA was associated with increased levels of HNP1-3 (β = 0.11; 95% CI: 0.02, 0.20) and LL-37 (β = 0.28; 95% CI: 0.08, 0.48).

CONCLUSIONS. This is the first study to highlight that cationic polypeptides investigated were increased in the CVS of HIV-negative women using DMPA. While some of these cationic polypeptides have intrinsic antiviral capacity, they may also promote recruitment of target cells for HIV infection and are associated with increased HIV virion load. This indicates that one potential mechanism for increased HIV risk associated with DMPA is the recruitment or activation of cells susceptible to HIV infection.

RESULTS

Cohort Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>None N=165</th>
<th>DMPA N=41</th>
<th>Oral N=16</th>
<th>Implant N=6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>28 (24, 34)</td>
<td>26 (24, 30)</td>
<td>27.5 (23, 33)</td>
<td>29 (24, 38)</td>
</tr>
<tr>
<td>HIV-2 seropositive</td>
<td>64 (37.3)</td>
<td>21 (52.5)</td>
<td>21 (52.5)</td>
<td>2 (33.3)</td>
</tr>
<tr>
<td>Sex acts in past month</td>
<td>5 (2.5, 8)</td>
<td>2 (5, 6)</td>
<td>6 (16.2, 25)</td>
<td>5 (2, 11.5)</td>
</tr>
<tr>
<td>Any unprotected sex</td>
<td>64 (38.6)</td>
<td>16 (39.0)</td>
<td>12 (30.0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Vaginal washing</td>
<td>40 (24.2)</td>
<td>16 (39.0)</td>
<td>3 (8.3)</td>
<td>2 (33.3)</td>
</tr>
<tr>
<td>Vaginal drying</td>
<td>27 (17.1)</td>
<td>7 (17.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Bacterial vaginosis</td>
<td>27 (17.1)</td>
<td>7 (17.1)</td>
<td>0 (0)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Desire additional children</td>
<td>87 (52.7)</td>
<td>23 (56.1)</td>
<td>12 (30.0)</td>
<td>1 (16.7)</td>
</tr>
<tr>
<td>PSA present</td>
<td>32 (14.3)</td>
<td>9 (22.0)</td>
<td>4 (10.0)</td>
<td>0 (0)</td>
</tr>
</tbody>
</table>

Levels of Cationic Polypeptides by Hormonal Contraceptive Use

No-Hormonal Contraception | DMPA | Oral | Implant

HNP1-3 (ng/ml) | 0.39** | 0.39** | 0.39** | 0.39**
Lactoferrin (LL-37) (ng/ml) | 0.39** | 0.39** | 0.39** | 0.39**

DISCUSSION

Higher levels of some innate immune factors (HNP1-3, LL-37) have been associated with increased HIV acquisition.4 This provides a potential biological link between DMPA use and HIV risk.

A mechanism for increased HIV risk with DMPA may be through immune modulation via recruitment of target cells or alteration of surface receptors.

Other studies found DMPA decreases IFNα and prevents down-regulation of CXCR4 and CCR5 on the surface of T cells.

DMPA appears to have a complex affect on the innate immune response in the vagina, with some factors up-regulated and others down-regulated.

Research is needed that looks collectively at the overall innate immune response rather than focusing on a small number of immune factors.

Large numbers of unplanned pregnancies demonstrate the need for long acting reversible contraception that is safe and acceptable.

Improving the method mix would provide more options to women with unplanned pregnancies.

REFERENCES


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