A comparison of Human Papilloma Virus infection and cervical cytology in women with copper and levonorgestrel containing intrauterine devices

Jovana Lekovic, Melissa K Frey, Misha Pangasa, Melanie Chan, Aneesha Varrey, Jolyon Taylor, Kevin Holcomb

Department of Obstetrics and Gynecology, New York Presbyterian Hospital Weill Cornell Medical College

ABSTRACT

Study Question: Is there a difference in the natural history of Human Papilloma Virus (HPV) infection and cervical cytology between women with copper and levonorgestrel containing intrauterine devices (IUD)?

Summary answer: The copper IUD and levonorgestrel IUD are equally associated with the development of atypical cells of undetermined significance (ASCUS) after the IUD placement in patients who had a normal cervical cytology before the placement; however the copper IUD was associated with higher HPV infection clearance rate compared to levonorgestrel IUD.

What is known already: Current literature suggests that cellular immune response triggered by copper IUD might act as a protective factor in cervical carcinogenesis by enhancing HPV infection clearance. To the contrary, a recent retrospective analysis suggested an increased risk of HPV persistence and progression of cervical dysplasia in progesterone-only method users. To our knowledge, this is the first study to compare the natural history of HPV infection and cervical cytology between users of the two types of IUD.

Study design, size and duration: Retrospective cohort study including 298 women who underwent IUD placement between 1/31/2006 and 1/31/2011. The mean duration of follow-up was 378 and 357 days for Levonorgestrel and Copper IUD groups respectively.

Materials and Methods: The electronic medical record system was searched by the appropriate procedural code for all patients undergoing IUD placement during the study period. HPV and cervical cytology results immediately preceding and following IUD placement were obtained.

Main results and the role of chance: 150 patients had a copper IUD placed, and 152 patients a levonorgestrel IUD. The groups were comparable in terms of age (mean 33.4±4.3 vs. 32.7±3.8 years), BMI, parity, duration of follow up and percentage of smokers (14% and 12% respectively). ASCUS was the most common cytologic abnormality to follow placement of an IUD (98% of all abnormalities). Copper and levonorgestrel IUDs were comparable in their rates of association with subsequent ASCUS Pap smears (5.9% vs. 3.0%, respectively, P = 0.38). 66 patients were HPV positive prior to IUD insertion (30 in levonorgestrel vs. 36 in copper IUD group). Of those, 21 (71%) cleared the infection following copper IUD placement compared with 15 (41%) in the levonorgestrel group (P = 0.02). Age and tobacco use were not associated with HPV infection persistence.

Limitations, reasons for caution: Main limitations of our study include its retrospective nature, small sample size, relatively short follow-up and inability to control for number of sexual partners.

Wider implications of the findings: Our data suggests that the copper IUD may promote clearance of HPV infection when compared with the levonorgestrel IUD. Copper IUD could potentially be the contraceptive method of choice and used as conservative treatment in women with persistent HPV infection or even cervical dysplasia. Both types of IUD are associated with a low rate of cervical cytology abnormalities, the majority being ASCUS.

BACKGROUND

• The effect of IUDs on natural history of HPV and cervical cancer remains unknown.

• Clinical and epidemiologic studies from several countries have reported inconsistent results.

• The largest meta-analysis suggests that the IUD might act as a protective cofactor in cervical carcinogenesis. However information on the type of IUD was not documented.

• Literature suggests that cellular immune response triggered by copper IUD might act as a protective factor in cervical carcinogenesis by enhancing HPV infection clearance.

• On the contrary, a recent retrospective analysis suggested an increased risk of HPV persistence and progression of cervical dysplasia in progesterone-only method users.

• To our knowledge, this is the first study to compare the natural history of HPV infection and cervical cytology between users of the two types of IUD.

METHODS

• Retrospective cohort study including 302 women who underwent IUD placement between 1/31/2006 and 1/31/2011.

• The mean duration of follow-up was 378 days.

• The electronic medical record system was searched by the appropriate procedural code for all patients undergoing IUD placement during the study period.

• HPV and cervical cytology results immediately preceding and following IUD placement were obtained.

RESULTS

Table 1: Patient demographics information and Pap smear/HPV results

<table>
<thead>
<tr>
<th></th>
<th>Levonorgestrel IUD</th>
<th>Copper IUD</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>150</td>
<td>152</td>
<td>NS</td>
</tr>
<tr>
<td>Age (years)</td>
<td>33.4±4.3</td>
<td>32.7±3.8</td>
<td>NS</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>22.1±4.8</td>
<td>23.2±5.2</td>
<td>NS</td>
</tr>
<tr>
<td>Smokers</td>
<td>18 (12%)</td>
<td>21 (14%)</td>
<td>NS</td>
</tr>
<tr>
<td>Mean # days between IUD placement and following Pap</td>
<td>378.6±38.2</td>
<td>357.4±32.1</td>
<td>NS</td>
</tr>
<tr>
<td>Mean # days between 2 Paps</td>
<td>554.9±22.1</td>
<td>534.6±29.2</td>
<td>NS</td>
</tr>
<tr>
<td>New ASCUS diagnosed after IUD placement</td>
<td>9 (5.9%)</td>
<td>5 (3%)</td>
<td>NS</td>
</tr>
<tr>
<td>HPV positive before IUD placement</td>
<td>30</td>
<td>36</td>
<td>NS</td>
</tr>
<tr>
<td>Cleared HPV on Pap after IUD placement</td>
<td>21 (71%)</td>
<td>15 (41%)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

CONCLUSIONS

• Our data suggests that the copper IUD may promote clearance of HPV infection when compared with the levonorgestrel IUD.

• Copper IUD could potentially be the contraceptive method of choice and used as conservative treatment in women with persistent HPV infection or even cervical dysplasia.

• Both types of IUD are associated with a low rate of cervical cytology abnormalities, the majority being ASCUS.

REFERENCES