Effects of Continuous Combined Oral Contraceptives on Mouse Mammary Gland Structure and Tumor Progression

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Supported by NIH grant # R21 CA170056

Abstract

The use of cyclical oral contraceptives (OC) is associated with an overall increased risk of ER+/- and ER- breast cancer. The role of estrous cycling in the development of mammary tumors is controversial. Theorized to contribute to breast cancer risk, estrous cycling may have no effect, or it may have an oncogenic role. Interacting factors may significantly influence the degree of estrous cycling and, therefore, may modify the risk of breast cancer development. In this study, we aimed to determine the influence of estrous cycling and the effect of estrous cycling on breast cancer risk and development.

Materials and Methods

Animals

BALB/c mice were purchased from Jackson Lab and aged 35 days at the beginning of the study. Mice were divided into two groups, continuously cycled and continuously fed, after the administration of a single injection of oral contraceptive (OC) or vehicle (control). Mice were weighed thrice weekly and had ad libitum access to food and water. Mice were sacrificed at the end of the study.

Table 1: Effect of OC on mammary gland structure.

<table>
<thead>
<tr>
<th>Time (days)</th>
<th>Control</th>
<th>Continuous</th>
<th>Cyclic OC</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>4</td>
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<td>0.2</td>
<td>0.4</td>
<td>0.001</td>
</tr>
<tr>
<td>6</td>
<td>0.2</td>
<td>0.4</td>
<td>0.6</td>
<td>0.002</td>
</tr>
<tr>
<td>8</td>
<td>0.4</td>
<td>0.6</td>
<td>0.8</td>
<td>0.003</td>
</tr>
<tr>
<td>10</td>
<td>0.6</td>
<td>0.8</td>
<td>1.0</td>
<td>0.004</td>
</tr>
<tr>
<td>12</td>
<td>0.8</td>
<td>1.0</td>
<td>1.2</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Results

Figure 1: Effect of OC on epithelial density.

The presence of both mammary gland and ductal lesions was observed in mammary glands from mice fed cyclic OC (P < 0.001). The number of ductal lesions was significantly higher in mice fed cyclic OC compared to control mice.

Figure 2: Effect of OC on tumor multiplicity.

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Figure 3: OC increases proliferation in the mammary gland.

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Figure 4: Both continuous and cyclic OC increase the cellular infiltration in the white adipose tissue.

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Figure 5: Effects of OC on palpable tumor burden and multinity.

Both continuous and cyclic OC decreased palpable tumor burden. Right: Despite initiating in a single site in the mammary fat pad, multiple lesions arose at the site of injection. Both continuous and cyclic OC decreased mammary tumor burden. Left: Both continuous and cyclic OC decreased mammary tumor burden. Right: Despite initiating in a single site in the mammary fat pad, multiple lesions arose at the site of injection. Both continuous and cyclic OC decreased mammary tumor burden.

Summary

- Both continuous and cyclic OC decreased mammary tumor burden.
- Mammary tumor burden was significantly lower in mice treated with OC compared to control mice.

References