Abstract

The use of oral contraceptive (OC) is associated with an overall increased risk of ER-positive breast cancer by 45% (for “ever-use” of OC) and of uterine cancer by as much as 8% (after 10 years of OC use) (reviewed in [12]). In contrast to its effects on endometrial and ovarian cancer risk, OC usage has not been shown to be a prevention agent for breast cancer. Although different studies involving various women, a meta-analysis calculates that overall, OC usage increases breast cancer risk by 1.24 (for current users) (1.0/1.4 years previously), and 1.09 (5-9 years previously) [13]. For current users, risk is further increased when the age at which she used OC was less than 25 years [12]. Suggesting that there may be an OC-sensitive developmental window soon after the onset of puberty where exposure to exogenous hormones can have long-lasting effects on BC risk, the authors have determined a functional cyclic-dynamin gene (RAS), whose expression is increased in breast tissue undergoing proliferation and epithelial cells, a potential risk of some breast cancer risk (7-9). It has been suggested that they are factors that regulate regular cycling decreasing breast cancer risk even in women who have never been on OC. Furthermore, taking OCs and oral contraceptives are linked to breast cancer risk. Late menstrual and early menopause are inversely associated with risk of breast cancer, increased oral contraceptive (OC) use increases the risk of breast cancer, and reduced breast cancer risk is associated with increased frequency of menstrual cycles and higher age at menopause. Therefore, the risk of breast cancer is associated with the number of menstrual cycles and higher age at menopause.

Materials and Methods

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Results

Table 1: Effects of OC on TM2H mammary tumor latency, survival and multiplicity.

- Both continuous and cyclical OC decreased palpable tumor burden. Right: Despite inclusion in a single site in the mammary fat pad, multiple lesions arose at the site of injection. Both cyclical and continuous OC use resulted in a marked increase in the size of palpable tumors, but continuous OC was associated with a trend (HES) to increased bulky complexity in paraffin sections (both OC regimen showed an effect on the number of % tumors). Both regimen increased % tumors. Responders represent % HES+ and % tumor burden. *P<0.05, ** P<0.005

Figure 5. Effects of OC regimen on palpable tumor burden and multiplicity. Left: Both continuous and cyclical OC decreased palpable tumor burden. Right: Despite inclusion in a single site in the mammary fat pad, multiple lesions arose at the site of injection. Both cyclical and continuous OC use resulted in a marked increase in the size of palpable tumors, but continuous OC was associated with a trend (HES) to increased bulky complexity in paraffin sections (both OC regimen showed an effect on the number of % tumors). Both regimen increased % tumors. Responders represent % HES+ and % tumor burden. *P<0.05, ** P<0.005

Figure 4. Both continuous and cyclical OC increase the cellular infiltration in the white adipose tissue. Top: Representative images from H&E-stained sections from mammary glands of mice fed control, continuous or cyclical OC. Bottom: The expression of CD31 and CD68, a macrophage cell marker. Both regimens increased expression of both CD31 (control and continuous OC) or CD68 (cyclical OC). Asterisks represent significant difference from control (P<0.05).

Figure 3. 5701-Tumor volume (mm3)

Figure 2. Effect of OC on mammary gland microarchitecture. Top: Representative images showing terminal structures in mammary glands of mice prepared from mice fed control, continuous or cyclical OC. Middle: Both continuous and cyclical OC regimens decrease the frequency of TEBs, and increase the frequency of epithelial buds (P<0.05). Terminal buds were unchanged in frequency. Bottom: Continuous OC is associated with a trend (HES) to increased bulk density in paraffin sections; both OC regimen show a trend (P<0.05) with increased % ducts with terminal buds. Asterisks represent % HES+ and % tumor burden. *P<0.05, ** P<0.005

Figure 1. Effect of OC on epithelial density. Top: whole mounts of mammary ductules for control (C), cyclical (Cyclical OC) and continuous (Continuous OC) groups. Histological images showing epithelial density in H&E-stained sections for control groups. Representative images showing epithelial density in H&E-stained sections for continuous and cyclical OC groups. H&E-stained sections showing epithelial density in H&E-stained sections for control and cyclical OC groups. *P<0.05, ** P<0.005

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References

- Both continuous and cyclical OC and all liver mammary gland structure (decreased TEBs). The number of mammary ductules increased (decreased adipose cell infiltration) when administered for seven days cycle post-puberty.
- Continuous OC increased epithelial density.
- Cyclical OC significantly increased epithelial periblobular proliferation.
- Only continuous OC increased tumor latency.
- Both OC regimens reduced tumor burden and multiplicity.
- Once tumors were established, OC did not affect tumor growth rate.

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