Effects of oral contraceptives on peak exercise capacity

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Casazza, Gretchen A., Sang-Hoon Suh, Benjamin F. Miller, Franco M. Navazio, and George A. Brooks. Effects of oral contraceptives on peak exercise capacity. J Appl Physiol 93: 1698–1702, 2002; 10.1152/japplphysiol.00622.2002.—We examined the effects of menstrual cycle phase and oral contraceptive (OC) use on peak oxygen consumption (VO2peak). Six moderately active, eumenorrheic women (25.5 ± 1.5 yr) were studied before and after 4 mo of OC. Subjects were tested during the follicular and luteal phases before OC and the inactive and high-dose phases after OC. Before OC, there were no significant differences between the follicular and luteal phases in any of the variables studied. There were also no differences between the inactive and high-dose phases. Dietary composition, exercise patterns, and peak heart rate, minute ventilation, and respiratory exchange ratio did not change with OC use. However, OC use significantly (P ≤ 0.05) increased body weight (59.6 ± 2.3 to 61.2 ± 2.6 kg) and fat mass (13.3 ± 1.3 to 14.5 ± 1.3 kg) and decreased VO2peak (−11%, 2.53 ± 0.21 to 2.25 ± 0.18 l/min). In conclusion, 1) endogenous ovarian steroids have little effect on VO2peak but 2) the exogenous ovarian steroids in OC decrease peak exercise capacity in moderately physically active young women.

PARTICIPATION BY WOMEN IN both recreational and competitive sports has increased dramatically over the last two decades. In addition, the US Surgeon General’s Report on Physical Activity and Health recommends that women of all ages, not just athletes, include a minimum of 30 min of moderate-intensity exercise on most days of the week (25). However, dietary energy insufficiency associated with high-intensity exercise training and competition can increase a woman’s risk of experiencing an abnormal menstrual cycle (3, 13). Abnormal menstrual cycles, with chronically low ovarian hormone levels, may increase the risk for osteopenia, osteoporosis, and fractures (7). Oral contraceptives (OCs) are used for birth control in normally menstruating young women, and, although controversial, OCs have been used to prevent bone loss in amenorrheic athletes (8, 16). However, there is concern among athletes that these exogenous ovarian hormones affect exercise performance.

Peak oxygen consumption (VO2peak) is considered the “standard” for assessing aerobic exercise capacity (23), and VO2peak in women could vary owing to ovarian hormone influences on stroke volume, pulmonary minute ventilation, oxygen-carrying capacity, blood flow, and muscle oxygen utilization. Although the cyclic endogenous ovarian hormone fluctuations across the normal menstrual cycle do not appear to affect VO2peak (1, 6, 12), low-dose administration of exogenous estrogen and progesterone may have a greater influence on exercise capacity. Only a few studies have examined the effects of exogenous steroids on exercise performance by use of longitudinal study designs. Although short-term OC use (21 days) did not affect VO2peak (2), 6 mo of monophasic OC use was associated with a significant decrease in VO2peak in endurance-trained women (18).

To our knowledge, no longitudinal studies have examined peak exercise capacity in moderately trained women before and after triphasic OC use. With monophasic OCs, the estrogen and progestin components remain constant throughout the pill cycle. In contrast, in triphasic OCs the amounts of estrogen and/or progestin vary across the pill cycle and more closely mimic the ovarian hormone variation that occurs during the normal menstrual cycle. Triphasic OCs contain lower per-cycle progestin levels to provide better cycle control and reduce the incidence of androgenic side effects such as alterations in carbohydrate and lipid metabolism (4) and therefore may not have the same influence on exercise capacity as monophasic OCs. The purpose of this investigation was to examine the effects of menstrual cycle phase (endogenous ovarian hormones) and triphasic OC use (exogenous ovarian hormone analogs) on peak exercise capacity, as measured by VO2peak.

MATERIALS AND METHODS

Subjects. Eight subjects were recruited from the University of California, Berkeley campus, to participate in a series of experiments to examine the effects of ovarian hormones on cardiorespiratory function and substrate utilization during peak and prolonged submaximal exercise. Results from the submaximal exercise trials on normally menstruating
ORAL CONTRACEPTIVES AND EXERCISE CAPACITY

Table 1. Physical characteristics of young women before and after 4 mo of OC

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before OC*</th>
<th>After OC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FP</td>
<td>LP</td>
</tr>
<tr>
<td>Age, yr</td>
<td>25.5 ± 1.5</td>
<td>25.5 ± 1.5</td>
</tr>
<tr>
<td>Height, cm</td>
<td>163.8 ± 1.9</td>
<td>163.8 ± 1.9</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>59.4 ± 2.3</td>
<td>59.8 ± 2.3</td>
</tr>
<tr>
<td>Body fat, %</td>
<td>21.8 ± 1.3</td>
<td>22.5 ± 1.5</td>
</tr>
<tr>
<td>Lean body mass, kg</td>
<td>46.4 ± 1.5</td>
<td>46.2 ± 1.4</td>
</tr>
<tr>
<td>Fat mass, kg</td>
<td>13.0 ± 1.2</td>
<td>13.6 ± 1.3†</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 women. FP, follicular phase; LP, luteal phase; IP, inactive phase; HP, high dose phase; OC, oral contraceptives. *Includes some of the same subjects as a previous report (22). †Significantly different from FP; ‡significantly different from LP, P ≤ 0.05.

Table 2. Ovarian hormone profiles before and after 4 mo of OC

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before OC*</th>
<th>After OC</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>FP</td>
<td>LP</td>
</tr>
<tr>
<td>Day of cycle</td>
<td>7 ± 0.7</td>
<td>21 ± 1.1</td>
</tr>
<tr>
<td>Days past ovulation</td>
<td>8 ± 0.6</td>
<td>34.1 ± 10.6†</td>
</tr>
<tr>
<td>Estradiol, pg/ml</td>
<td>0.38 ± 0.04†</td>
<td>10.6 ± 2.4</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 women. Day of cycle, days after start of menses before OC and day of pill cycle with OC. *Includes some of the same subjects as a previous report (22). †Significantly different from LP, P ≤ 0.05.
There were no significant differences in body weight or the phase criteria for every experimental protocol. Our laboratory because not all of the eight subjects met are presented in Table 1. Subject numbers and character-

<table>
<thead>
<tr>
<th>Variable</th>
<th>Before OC</th>
<th>After OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Power output, W</td>
<td>175 ± 14.4</td>
<td>150 ± 12.4†‡</td>
</tr>
<tr>
<td>Time, min</td>
<td>14 ± 1.5</td>
<td>12 ± 1.5†‡</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>192 ± 4.2</td>
<td>192 ± 3.6</td>
</tr>
<tr>
<td>VE, l/min</td>
<td>78.9 ± 5.3</td>
<td>79.4 ± 2.3</td>
</tr>
<tr>
<td>Peak VO₂, l/min</td>
<td>2.51 ± 0.20</td>
<td>2.25 ± 0.19†‡</td>
</tr>
<tr>
<td>Peak VO₂, ml·kg⁻¹·min⁻¹</td>
<td>42.3 ± 3.3</td>
<td>36.9 ± 2.9†‡</td>
</tr>
<tr>
<td>Peak VCO₂, ml·kg⁻¹·min⁻¹</td>
<td>54.1 ± 4.1</td>
<td>48.1 ± 4.0†‡</td>
</tr>
<tr>
<td>RER</td>
<td>1.18 ± 0.01</td>
<td>1.16 ± 0.03</td>
</tr>
</tbody>
</table>

Values are means ± SE for 6 women. VO₂, oxygen consumption; VE, pulmonary ventilation; VCO₂, carbon dioxide production; RER, respiratory exchange ratio; LBM, lean body mass. *Includes some of the same subjects as a previous report (22). †Significantly different from FP; ‡significantly different from LP, P < 0.05.

RESULTS

Subject characteristics. Subject characteristics for the six women that met the ovarian hormone criteria on the day of maximal exercise testing, for all phases, are presented in Table 1. Subject numbers and characteristics vary between the series of reports (22) from our laboratory because not all of the eight subjects met the phase criteria for every experimental protocol. There were no significant differences in body weight or body composition between FP and LP before OCs or between IP and HP with OCs, except a slightly higher fat mass in LP vs. FP. However, there was a small, but significant (P < 0.05), increase in body weight (3%) and fat mass (9%) after 4 mo of OC use.

There were no significant changes in total energy intake (1,920 ± 191 kcal before OC and 1,819 ± 260 kcal after OC), percentage of the energy intake as carbohydrate (58 ± 2.2% before OC and 54 ± 2.9% after OC), percentage of the energy intake as fat (27 ± 2.9% before OC and 31 ± 3.1% after OC), and percentage of the energy intake as protein (15 ± 1.6% before OC and 14 ± 1.3% after OC) with OC use.

Day of cycle, days past ovulation, and the ovarian hormone profiles for each phase are shown in Table 2. Criteria for FP (progesterone < 1 ng/ml) and LP (progesterone > 3 ng/ml) were met in six subjects before OC use. LP was associated with significantly higher (P < 0.05) estradiol and progesterone concentrations than all other phases. Both ovarian hormones were low after OC use, validating the suppression of endogenous hormone production by synthetic ovarian steroids.

Cardiorespiratory responses. At peak effort, there were no significant differences in any of the cardiorespiratory variables between FP and LP before OC use or between IP and HP with OC (Table 3). However, after 4 mo of OC use, there were significant decreases (P < 0.05) in time to peak exercise (14%) and in the peak power output attained (8%). There were also significant (P < 0.05) reductions in VO₂ peak measured in both liters per minute (11%) and milliliters per kilogram per minute (13%) and in peak carbon dioxide production (15%). There were no significant changes in peak heart rate, pulmonary minute ventilation, and respiratory exchange ratio. All six subjects experienced a decline in VO₂ peak (ml·kg⁻¹·min⁻¹) after 4 mo of OC use (Fig. 1).

DISCUSSION

This study confirms that, in the absence of OCs, menstrual cycle phase does not affect peak exercise capacity, with no significant changes in body weight, body composition, or cardiorespiratory factors, including VO₂ peak, between the follicular and luteal phases. However, 4 mo of a low-dose triphasic OC resulted in a significant increase in body weight and fat mass and a significant 11% decrease in VO₂ peak not normalized to body mass. There was no change in VO₂ peak between the inactive and high-dose phase with OCs, suggesting a persistent synthetic ovarian hormone effect despite a 1-wk cessation of ovarian steroid intake between cycles.

That OCs, but not luteal phase menstrual cycle variations in ovarian hormones, affected VO₂ peak suggests that steroid levels may be involved in suppression of peak exercise capacity. OCs mimic the estrogen profile...
during pregnancy, with high levels of ethinyl estradiol (>300 pg/ml), levels that are much higher than observed during the normal menstrual cycle (24). As well, the type of contraceptive pill may have an effect on $V_{O_2 \text{peak}}$. Our finding of an 11–13% decrease in $V_{O_2 \text{peak}}$ in moderately trained women after 4 mo of triphasic OCs is greater than the 7% decrease in $V_{O_2 \text{peak}}$ found in endurance-trained women with 6 mo of monophasic OCs (18). Moreover, C. M. Lebrun (unpublished observations) has observed a similar, small, but statistically significant decrease in $V_{O_2 \text{peak}}$ with triphasic OC use in athletic women. And, finally, the duration of OC use may play a role. Longer than 1 mo of OC use appears to be necessary to induce physiological changes because a study examining 1–3 wk of monophasic OCs found no significant effect on $V_{O_2 \text{peak}}$ (2).

Although the number of subjects was small in our investigation, every subject experienced a drop in $V_{O_2 \text{peak}}$ with OC use, indicating a significant physiological effect. That $V_{O_2 \text{peak}}$ was depressed during both IP (ethinyl estradiol levels ≈ 8 pg/ml) and HP (ethinyl estradiol levels > 300 pg/ml) phases of OC use is taken to indicate persistence of OC effects (24). In agreement with our findings are those of Lynch et al. (14), who looked at the effects of long-term OC use on intermittent exercise performance in untrained women.

Factors that could reduce $V_{O_2 \text{peak}}$ include decreases in stroke volume, oxygen-carrying capacity (hemoglobin levels), muscle blood flow, or oxygen extraction or changes in the pattern of substrate utilization. However, most of these do not appear to be candidates for an OC-induced negative effect on $V_{O_2 \text{peak}}$. A decrease in stroke volume is unlikely because estrogen replacement therapy has been shown to increase stroke volume (10) and OC use has been shown to increase the activity of the renin-angiotensin-aldosterone system at rest (19). Decreased hemoglobin concentration is also unlikely because most studies have found no difference in resting blood hemoglobin and ferritin concentrations (11, 17) and an increase in serum iron levels (17) with OC use, presumably owing to a decrease in menstrual blood loss (11).

Although we did not directly assess sympathetic nervous system activity (SNA) in this study, decreased SNA and plasma catecholamine concentrations could explain the lower peak oxygen consumption observed with high ovarian hormone concentrations. Consistently high estrogen and progesterone concentrations, such as occur during pregnancy and with exogenous ovarian hormones, may blunt SNA and catecholamine levels as a protective mechanism to maintain blood flow to the uterus and prevent maternal hypoglycemia and uterine contractions (15).

Both the sympathetic nervous and endocrine systems play roles in maintaining normal blood glucose concentrations. Because catecholamines do not begin to rise in the circulation until the level of effort becomes strenuous (e.g., >65% $V_{O_2 \text{peak}}$), catecholamines are directly involved in glycogen mobilization during strenuous exercise. In contrast, hormones such as human chorionic somatotropin, growth hormone, cortisol, and thyroid hormone play roles in maintaining glucose homeostasis during pregnancy (15), and their importance is more likely exhibited during submaximal prolonged exercise. However, catecholamines are directly involved in hepatic and muscle glycogen mobilization during strenuous exercise. The fetus relies almost exclusively on maternal glucose for growth and development (15), and suppression of epinephrine and norepinephrine release could be a means of preventing maternal liver glycogen depletion and low blood glucose concentrations.

Pregnancy is associated with suppressed catecholamine levels during strenuous exercise (15), and exogenous estradiol administration has been shown to decrease SNA at rest (26), decrease catecholamine levels and glucose production and utilization during exercise (20), and increase the levels of the potent vasodilator nitric oxide (5). During exercise, increased SNA and the resultant vasoconstriction in nonactive tissue is essential for increasing blood flow to the working muscle. As exercise intensity increases, some vasoconstriction in the active muscle is also required to maintain mean arterial pressure. Blunting of SNA with high ovarian hormone concentrations, therefore, could limit peak exercise performance.

Although oral contraceptives decrease peak exercise capacity in moderately trained young women, effects of these synthetic steroid hormones on prolonged endurance exercise performance in competitive athletes are less obvious and warrant further investigation. The decrement in $V_{O_2 \text{peak}}$ induced by OC use may subside over time or become insignificant owing to training-induced adaptations in highly trained female athletes.

In conclusion, these results suggest that 1) endogenous hormones have little effect on exercise performance as measured by $V_{O_2 \text{peak}}$, but 2) low-dose triphasic OCs (exogenous ovarian hormones) appear to decrease peak exercise performance in moderately physically active young women.

NOTE ADDED IN PROOF

The number of subjects we studied was small, but similar results on the effects of OCs on $V_{O_2 \text{max}}$ are reproducible. Since acceptance of our paper, we have learned that the work of Lebrun et al., cited as unpublished, is now in press (Lebrun CM, Petit MA, McKenzie DC, Taunton J, and Prior JC. Decreased $V_{O_2 \text{max}}$ with triphasic oral contraceptive use in highly active women: a randomised controlled trial. Br J Sports Med In Press.

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