Effects Of Oral Contraception
On Serum Lipids And
Vitamin-E Levels

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SUMMARY
The action of oral contraceptives (OC) (50 mg ethinylestradiol + 500 μg norgestrel) on serum lipids, total cholesterol and vitamin-E levels was studied in two groups of women who took this OC for 12 months, or for a longer period of time (13 months to 7 years). Comparison with the control group showed that the ingestion of OC elevates serum total lipid and cholesterol. This increase was more marked in the women who took this OC for a longer period of time. In addition to this, a significant increase was determined in vitamin-E levels in group II, whereas it was not altered in group I. We observed no change in vitamin-E/total lipid ratio in both groups, but a significant elevation was determined in vitamin-E/total cholesterol ratio in group II. It was suggested that this dose of OC induces changes in the lipid profile and vitamin-E concentration in long term OC users.

Keywords: Contraception, vitamin-E, total cholesterol, total lipids.

INRODUCTION
A number of metabolic effects due to the use of oral contraceptives have been reported, including alterations in the nutritional status of several vitamins and lipid metabolism. Information on the effects of oral contraceptives on vitamin-E levels is conflicting. While some workers have reported no alteration (1,2) or a fall (3), a small but significant increase was observed by Smith et al (4).
Effects of Oral Contraception on Serum Lipids and Vitamin-E Levels

**Table - I**

**Plasma Vitamin-E Total Cholesterol And Total Lipid Levels (Mean ± SD) In Women Taking Oral Contraceptives And Control Group**

<table>
<thead>
<tr>
<th></th>
<th>Vitamin-E (mg/dl)</th>
<th>Total cholesterol (mg/dl)</th>
<th>Total lipid (mg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Group (n = 32)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.843 ± 0.258</td>
<td>176.61 ± 32.59</td>
<td>654.43 ± 175.21</td>
</tr>
<tr>
<td><strong>OC Group I, 1 year (n = 12)</strong></td>
<td>0.925 ± 0.169 (P&gt;0.05)</td>
<td>209.16 ± 40.75 (P&lt;0.02)</td>
<td>778.66 ± 105.90 (P&lt;0.01)</td>
</tr>
<tr>
<td><strong>OC Group II, &gt; 1 year (n = 13)</strong></td>
<td>1.135 ± 0.320 (P&lt;0.01)</td>
<td>204.33 ± 29.34 (P&lt;0.02)</td>
<td>809.83 ± 98.30 (P&lt;0.001)</td>
</tr>
</tbody>
</table>

**Table - II**

**Plasma Vitamin-E, Total Cholesterol and Vitamin-E/Total Lipid Ratios in Women Taking Oral Contraceptives And Control Group**

<table>
<thead>
<tr>
<th></th>
<th>Vitamin-E/ total cholesterol</th>
<th>Vitamin-E vs. total cholesterol</th>
<th>Vitamin-E/ total lipid</th>
<th>Vitamin-E vs. total lipid</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Control Group (n = 32)</strong></td>
<td>4.77</td>
<td>0.235 NS</td>
<td>1.28</td>
<td>0.335 NS</td>
</tr>
<tr>
<td><strong>OC Group I, 1 year (n = 12)</strong></td>
<td>4.42</td>
<td>0.512 NS</td>
<td>1.18</td>
<td>0.390 NS</td>
</tr>
<tr>
<td><strong>OC Group II, &gt; 1 year (n = 13)</strong></td>
<td>5.55</td>
<td>0.604 (P&lt;0.05)</td>
<td>1.40</td>
<td>0.376 NS</td>
</tr>
</tbody>
</table>

n = Number of Subjects, NS = Non Significant.

Sidered to be the most reliable index of vitamin-E status (6). Although the effects of OC is not completely defined with respect to the serum lipids, it seems that progestins produce a decrease in triglycerides and HDL-cholesterol, while estrogens induce an increase in both parameters above; however this tendency may vary according to the dosage and of progestin and estrogens administrated (7).

In this study, an attempt was made to determine the effects of combined-type oral contraceptives (50 jg ethinylestradiol + 500 jg norgestrel) on the serum vitamin-E, cholesterol and total lipid levels in women. Particularly the effect of duration of ingestion (one year and longer) was examined.

**MATERIAL VE METOD**

A total of 57 fertile women attending Erciyes University Medical School, Department of Obstetrics and Gynaecology were investigated. There were 25 women in the age range 18-36 years (mean ± S1) =48 ± 4.07) who were taking a combination type of oral contraceptive, norgestrel 0.5 mg and ethinylestradiol 50 jg for a period of one year and longer. Twelve of these 25 women had taken this dosage for 12 months (group I) and the other 13 for a longer period of time (13 months ± 7 years). Thirtytwo women were selected to form a control group whose ages, diets and smoking habits were similar to the study group. Fasting blood samples were collected from all subjects and the plasma separated and stored at -20°C until studied. Plasma vitamin-E was estimated by the spectrophotometric method of Rindi (8). Plasma total cholesterol was determined by the method of Boyle-Zack (9) and total lipids using phosphovanilin method (10).

Student’s test and correlation analysis were used for statistical purposes.

**RESULTS**

Plasma vitamin-E, total cholesterol and lipid concentrations were shown in Table 1. No significant difference was determined between group I and control but the differences in total cholesterol, vitamin-E and total lipid levels between group II and control, and group I and group II were statistically significant (P < 0.01).

The ratios of vitamin-E to total lipids (1.28), and cholesterol (4.77) were similar with group I and control, but vitamin-E to total lipid (1.4) and...
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Table-III

Tentative Summary of Different Studies Concerning Effects of Diverse Combinations of Ethinylestradiol and Gonane Progestogens on Vitamin-E and Lipinds

<table>
<thead>
<tr>
<th>Type of OC (mg/day) and Investigators</th>
<th>Total cholesterol</th>
<th>Total lipid</th>
<th>Vitamin-E (Tocopherol)</th>
<th>Usage Period</th>
</tr>
</thead>
<tbody>
<tr>
<td>EE 50 + NE 1000 (4)</td>
<td>No change</td>
<td>Increased</td>
<td>Increased</td>
<td>2 years</td>
</tr>
<tr>
<td>EE 50 + NG 500 (12,13)</td>
<td>Increased</td>
<td>Increased</td>
<td>No change</td>
<td>1 year</td>
</tr>
<tr>
<td>EE 50 + NG500 (17)</td>
<td>No change</td>
<td>No change</td>
<td>No change</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td>EE 50 + NG 500 (18,19,20)</td>
<td>Increased</td>
<td>No change</td>
<td>Increased</td>
<td>&gt; 1 year</td>
</tr>
<tr>
<td>EE 50 + NG (In our study)</td>
<td>Increased</td>
<td>Increased</td>
<td>No change</td>
<td>1 year</td>
</tr>
<tr>
<td>EE 50 + NG 500 (In our study)</td>
<td>Increased</td>
<td>Increased</td>
<td>Increased</td>
<td>&gt; 1 year</td>
</tr>
</tbody>
</table>

EE = Ethinyl Estradiol; NG = Norgestrel; NE = Norethindrone

Discussion

Until rather recently, most of the literature on the suspected alterations in lipid metabolism associated with OC use was mainly concerned with products containing 1 to 10 mg of progestogen and 50 to 150 μg of either ethinylestradiol or mestranol. Although many of these studies are prospective, they differ widely in protocol, duration of IC use, nature of lipoproteins and lipids studied, statistical evaluation and characteristics of the subjects tested. A careful review of most of the recent studies devoted to that subject has been made by Fotherby (11).

In our study, we observed that although there was a significant increase in total cholesterol and lipid levels in OC users for one year (group I) and longer (group II), there was no statistically significant increase in vitamin-E levels in group I. It was determined that vitamin-E levels increased after a continuous usage period greater than one year. Our findings except total cholesterol are in good agreement with Smith’s et al.’s (4) findings. In addition to this, our data is also supported by Mendoza (12) and Briggs et al.’s (13) findings (Table 3).

In our study, we also observed that when tocopherol status is evaluated by the tocopherol/total lipid ratio for one year or longer period no change occurs. On the other hand, when tocopherol/total cholesterol ratio is examined, we obtained a significant increase after a continuous administration period greater than one year. According to this result, it is thought that amount of increase in tocopherol level is greater than total cholesterol with respect to control and group I. Our results are also concordant with Tagahashi’s observation that the best correlation of vitamin-E is with the serum cholesterol in group II (14).

One of biochemical effects of the estrogen component of oral contraceptives is on protein synthesis. Several enzymes can be induced in the liver of animals by the administration of estrogen compounds. Also, the profound changes that occur in the serum proteins in pregnant women are well known. Smith et al. (4) have been reported that
pseudopregnancy state created by oral contraceptives is associated with similar changes in serum proteins.

In humans vitamin-E is transported in the plasma within lipoproteins (5). No specific lipoprotein functions as one and only carrier of the vitamin, but rather the vitamin is distributed among all of the lipoproteins, with a large proportion in the low density lipoprotein fraction (15). In this respect, Traber et al (16) have demonstrated that a high affinity receptor for LDL functions as a mechanism for the delivery of vitamin-E to cells. They also showed that the LDL receptor-negative fibroblasts from patients with homozygous form of familial hypercholesterolemia did contain a measurable amount of tocopherol and presence of LDL in the medium resulted in an increase in tocopherol content of these fibroblasts. They suggested that the LDL receptor mechanism was not the only mechanism for delivery of tocopherol to cells.

In our study, we observed that OC administration for a longer period than one year, causes an elevation in vitamin-E levels. Since serum or plasma vitamin-E levels are closely related to the amounts of vitamin-E binding lipoprotein fraction of mucosal and liver cytosol and serum, it may be suggested that any increase in the amounts of this fraction due to the action of estrogens may also cause an elevation in transported vitamin. Besides this, LDL-receptor or another mechanism for absorption of tocopherol may also be stimulated by estrogens in mucosal cells of the intestine. In a further study, it may have been useful to gather detailed data about LDL-receptor mechanism for absorption of vitamin-E under the influence of oral contraceptives.

In conclusion, the high dose combination ethinyl estradiol 50 µg plus norgestrel 500 µg clearly changes the lipid profile and vitamin-E concentrations in long term users.

REFERENCES


