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

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ORAL KONTRASEPTİVLERİN SERUM LİPİD VE E-VİTAMİNİ DÜZEYLERİ ÜZERİNE ETKİLERİ

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SUMMARY

The action of oral contraceptives (OC) (50 mg ethinylestradiol +' 500)Lg 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 montfts to 7 years). Comparison with die control group showed that the ingestion of OC elevates serum total lipid and cholesterol. This increase was more marked in die women who took Uus OC for a longer period of time. In addition to this, a significant increase was determined in vitamin-E levels in group II, where as it was not altered in group I. We observed no change in vitamin-Eltotal lipid ratio in bodi groups, but a sigitificant elevation was determined in vitamin-Eltotal cholesterol ration in g/roup 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, vilamin-E, total cholesterol, total lipids.**

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ÖZET

Bu çalışmada, bir yıl (grup 1) daha uzun süreli (grup 11,13 ay-7yd arası) arat kontraseptiv (50 jxg) etinilöstradiol + 500 yg norgestret) kullanan kadınların senim vitamin-E ve lipid düzeyleri tayın edildi. Kontrol grubu ite karşılaştırdığında, I. grupta total kolesterol ve total lipid değerlerinin anlamlı derecede yüksek olduğa, vitamin-E düzeyinin ise değişmediği gözlendi. II. grupta ise total kolesterol, lipid ve vitamin-E düzeyleri anlamlı olarak yüksek bulundu. Çalışma gruplannda,- tokoferol/total lipid oranında bir değişme olmadığı ancak uzun süreli oral kontraseptiv kutlananlarda vitamin-Eltotal kolesterol oranında anlamlı derecede artma olduğu izlendi. Uzun süreli olarak kullanılan bu dozda oral kontraseptivterin lipid profilinde »« vitamin-E düzeylerinde değişmeler yaptığı sonucuna vanldı.

Anahtar Kelimeler: **Kontrasepttvlcr, vitamin-E, total kolesterol, total lipid.**

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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).

In man, the major part of vitamin-E is transported by beta-lipoproteins, and a high coefficient of correlation has been reported between plasma vitamin-E and beta-lipoprotein concentrations (5), and between vitamin-E and total lipids (1).

Relating the plasma vitamin-E concentration to the tocopherol transport capacity, expressed as plasma lipid level (cholesterol, total lipids) is con-

Table -1

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

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

Table - II

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

	Vitamin-E/ total cholesterol	Vitamin E v.s.e total cholesterol	Vitamin-E/ total lipid	Vitamin-E v.s. total lipid
		r		r
Control Group (n = 32)	4.77	0.235 NS	1.28	0.335 NS
OC Group I, 1 year (n = 12)	4.42	0.512 NS	1.18	0.390 NS
OC Group II, > 1 year (n = 13)	5.55	0.604 (P<0.05)	1.40	0.376 NS

n = Number of Subjects, NS = Non Sigificant.

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 jxg ethinylestradiol + 500 jxg 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.

MATERYAL 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 ± SI) =48 ± 4.07) who were taking a combination type of oral contraceptive, norgestrel 0.5 mg and ethinylestradiol 50 jxg 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). Thirlytwo 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

Table-III

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

Type of OC (mg/day) and Investigators	Total cholesterol	Total lipid	Vilamin-E (Tocopherol)	Usage Period
EE 80 + NE 1000 **(4)**	No change	Increased	Increased	2 years
EE 50 + NG 500 (12,13)	Increased	Increased	–	1 year
EE 50 + NG5O0 **(17)**	No change	No change		1 year
EE 50 + NG500(17)	Increased	No change	–	> 1 year
EE 50 + NG 500 (18,19,20)	Increased	Increased	–	?
EE 50 + NG (In our study)	Increased	Increased	No change	1 year
EE 50 + NG 500 (In our study)	Increased	Increased	Incerased	> 1 year

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

vitamin-E to total cholesterol (5.55) were higher in group II than group I, and control groups(Tablc 2).

Correlations between vitamin-E and cholesterol or total lipids were also calculated. While vitamin-E levels were significantly related to cholesterol in group II ($r = 0.604$, $p < 0.05$), no correlation was obtained in control and group I. There was also no correlation in the control, group I and group II (Table 2). There were 16 women (64%) who had total serum lipid levels greater than 700 mg/dl, 4 women greater than 900 mg/dl (16%) totally in both groups.

DISCUSSION

Until rather recently, most of the literature on the suspected alterations in lipid metabolism associated with OC use was mainly conserned with products containing 1 to 10 mg of progestogen and 50 to 150 jxg of either ethinylestradiol or menstranol. Althogh 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).

Table 3 represents an attempt to synthesize the results obtained by different investigators and to indicate the statistically significant changes observed for total cholesterol, lipids and vitamin-E, when there was a consensus among the studies. In addition to these investigators, Jagadeesan et al (2). Suggested that compared to controls, plasma vitamin-E, cholesterol and total lipids were not altered in OC users. However, they did not give any detailed data about duration and type of the OC used.

In our study, we observed that although there was a significant incrase in total cholesterol and lipid levels in OC users for one year (gorup 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 Brigs 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 been demonstrated that a high affinity receptor for LDL functions as a mechanism for the delivary 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 delivary of tocopherol to cells.

In our study, we observed that OC administration for a longer period than one year, causes an elevatin 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 an 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 usefull to gather detailed data about LDL-receptor mechanism for absorbtion of vitamin-E under the influence of oral contraceptives

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

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