EFFECTS OF ORAL CONTRACEPTIVE ON ALPHA I-ANTI TRYPSIN ACTIVITY

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Human plasma is known to contain at least 6 inhibitors of enzyme, acting on proteins (Heimburger *et al*, 1971). Jacobsson (1955) first showed that about 90% of the inhibiting capacity remains in Alpha-I zone and rest 10% in Alpha-2 band.

Recently, Alpha 1- antitrypsin (Alpha 1-AT) enzyme deficiency has been associated with lung and liver disorders (Eriksson, 1965; Lieberman *et al*, 1971; Kishore *et al*, 1976). Kueppers (1968) was able to increase the levels of the enzyme by typhoid-vaccine. Lieberman *et al* (1971) reported high serum trypsin inhibitor capacity (SITC) values in Alpha-1 AT enzyme deficient subjects, when they were put on Diethylstilbestrol therapy.

Following such observations, the present study was undertaken to observe the effect of Ovlar on Alpha 1-AT activity.

Material and Methods

Fifty healthy females, who attended family welfare Clinic, were selected for the present study. They were examined in detail and those having any disease related with lung or liver were excluded. Alpha 1-Anti trypsin activity was measured before starting oral contraceptive therapy. They were provided oral pills (Ovlar having Ethynylestradiol 0.05 mg and Norgestrel 0.5 mg) for successive 3 months and were advised to visit every month for check up.

3 ml blood was taken in dry plain sterilized vials. Sera were separated. Alpha 1-Antitrypsin enzyme was estimated by Agar-Gel electrophoresis, using the method of Laurell and Eriksson, 1963). Serum-trypsin inhibiting capacity was measured by method of Eriksson (1965) using BAPNA-Hcl as substrate. Methods were the same as used in our previous study (Kishore *et al*, 1976). Normal Alpha 1-AT activity was assessed in a subject having 190 mg% Alpha 1-AT enzyme concentration and SITC 0.84 mg/ml inhibited trypsin. The subjects having < 190 mg% Alpha 1-AT enzyme and STIC < 0.84 unit were labelled as enzyme deficient subjects.

Heterozygous and homozygous enzyme deficiency were considered using the qualtitative and quantitative criterias of Lieberman *et al* (1971).

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Results

Mean levels in 50 healthy females, before oral contraceptive therapy were 278 mg% (96-412 mg%). Mean Alpha 2-MG concentration was 445 ± 76.5 (156-582 mg). The range of STIC was (0.56-1.31/ ml) with a mean of 1.16 ± 0.12 units.

Mean values ± S.D. of Alpha 1-AT, Alpha 2-MG and ST ± C values in 50 healthy females, before and after oral contraceptive therapy for subsequent 3 months are given below:

	Alpha I-At (mg%)	Alpha 2-Mg (mg%)	SITC (units)
Before therapy	278 ± 33	445 ± 76.3	1.16 ± 0.12
After 1st month	292 ± 54.5	476 ± 88.7	1.18 ± 0.21
After 2nd month	306 ± 47.8	493 ± 66.6	1.21 ± 0.17
After 3rd month	318.7 ± 7.51	517 ± 89.0	1.24 ± 0.11
	P <.01	P <.05	P <.01

Oral contraceptive significantly affected the concentration of Alpha 1-AT activity after 3 months. Alpha 1-AT, Alpha 2-Mg and STIC values increased significantly ($P < .01$).

Out of 50 females, one was having Alpha 1-AT enzyme deficiency. She was heterozygous for the enzyme deficiency.

Alpha 1-AT enzyme deficiency in 50 healthy females is given below:

Age Group	Total No.	Enzyme Deficiency		
		Total	Hetero-zygous	Homozy-gous
15-20	21	1 (2%)	1 (2%)	—
21-30	19	—	—	—
31-40	10	—	—	—

The deficient subject was having 96 mg% Alpha 1-AT concentration and after 3 months use of oral contraceptive pills, the enzyme values increased significantly.

The enzyme activity in a deficient subject before and after the use of oral pills is given below:

Before Therapy		After Therapy		
		1st month	2nd month	3rd month
Alpha I-AT (mg%)	96	124	156	172
STIC (Units)	0.56	0.62	0.73	0.78

Discussion

Alpha 1-AT is a low M.W. glycoprotein (55000-60000) and it constitutes some 3% plasma-proteins. It is synthesized in the liver and has the capacity to inhibit a variety of proteolytic enzymes (Heim-

burger *et al*, 1971) Deficiency of the enzyme is thought to be inherited, as an autosomal codominant gene (Fagerhol and Laurell, 1967).

The association of Alpha 1-AT deficiency with lung and liver diseases has opened up many avenues of research. The interesting aspect is to find out the ways and means to increase the levels of the enzymes in deficient subjects.

In the present series, the effect of Ovlar was studied on Antitrypsin activity. Insignificant rise of enzyme levels ($P<.05$) was observed at the end of the first month, but later, the enzyme concentration in the serum significantly increased. One enzyme deficient female, having serum Alpha 1-AT (96 mg%) showed a significant rise in enzyme values i.e. 172 mg% at the end of 3 months. STTC was also increased significantly i.e. from 0.56/ml to 0.78/ml, after 3 months use of Ovlar. Robertson (1967), previously noted the increase of Alpha 1-Globulin concentration in serum in those women who were taking oral contraceptives. Recent studies of Lieberman *et al* (1971) have confirmed the role of female-sex hormonoes in stimulating the liver to produce more enzyme. Diethylstilbestrol, in doses of 3 mg daily for 21 days, proved to be a potent stimulus for the enzyme synthesis.

How this effect is mediated, is not well known. The possibility of a direct effect on hepatic metabolism, following oestrogenic administrations have been stressed by many investigators. It may equally be possible that the response of Alpha 1-AT activity to female sex hormones, is a part of more or less general response of blood protein synthesis to the hormones. Thus, it seems that oestrogenic medication seems to have a potential value, as therapy for curing the antitrypsin deficiency. Heterozygous subjects responded very well to this therapy. How far these measures would prove useful in homozygous Alpha 1-AT deficiency, is a moot point. A large study is needed to elucidate the exact mechanism, responsible for the effects of female sex hormones on Alpha 1-Anti trypsin activity in the body.

Summary

Alpha 1-Anti trypsin activity was measured in 50 healthy females. Mean levels of the enzyme were 278 mg%. One female was having heterozygous enzyme deficiency (90 mg%). Ovlar (Norgestre 0.5 mg + Ethinylestradiol 0.05 mg) was given to these females for 3 months and it was found that there was a significant rise ($P < .01$) in the concentration of Alpha-I-AT activity. Enzyme deficient subject responded very well to this therapy. The significance of these observations have been discussed.

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