ALPHA-FETOPROTEIN ASSAY IN PATIENTS TREATED WITH LOW-DOSE ORAL CONTRACEPTIVES

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SUMMARY

AFP has proven to be a useful marker for liver neoplasms. The Authors assaied AFP plasma levels in patients taking low-dose estroprogestinics. Patients were divided into three groups on the basis of their living habits. No difference was found in any group between AFP levels before and after treatment. However, in the group of smokers using oral contraceptives AFP levels were significantly higher.

The increased incidence of liver misfunctioning in patients taking estroprogestinics has been fully demonstrated in research works by many Authors ([1, 2]). Besides changes in functional tests and higher incidence of cholelithias, concern has been aroused by reports ([3, 4, 5, 6, 7]) of liver neplasms in patients treated with estroprogestinics. Although their incidence does not exceed 0.5/100,000 these forms are rather significant as they are asymptomatic and their first sign can be sudden and lethal haemorrhagia ([8, 9]). Consequently several researchers have tried to find a way to detect this pathology as early as possible. As alpha-fetoprotein (AFP) has proven to be a useful marker for benign or malignant liver neoplasms ([10, 11, 12, 13]) assays of this protein have been made to find evidence of liver misfunctioning in patients treated with estroprogestinics. We have therefore assaied AFP plasma levels in women taking low-dose estroprogestinic preparations.

MATERIAL AND METHODS

We examined 150 patients who came to our day-centers for advice on oral contraception. Their age ranged between 18 and 40 years. All these patients underwent the usual tests' for detecting changes in the hepato-biliary function. We excluded patients with previous liver pathologies on the basis of anamnesis and hematochemical tests. Our study concerned therefore 110 patients who were subdivided into three groups on the basis of some living habits.

Group 1 included women only taking oral contraceptives (OC); group 2 those who took oral contraceptives and smoked 10 or more sigarettes per day (OC+smoke); group 3 included patients using oral contraceptives and taking alcoholic drinks as a habit (OC+alcohol).

Serum AFP was assaied in all patients before treatment started; the second assay was carried out after a period of therapy with estroprogestinics lasting from 24 to 36 months. We used an estroprogestinic preparation containing 0.15 mg Norgestrel and 0.03 mg Ethynylestradiol.

The data obtained were statistically analyzed according to the variance method; all changes in AFP levels in the three groups before and after estroprogestinic treatment were compared and differences between the various groups studied.

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Table 1. — *AFP plasma levels in patients treated with low-dose estroprogestinics.*

Groups	No. cases	Time of assay	Mean	ng % ml	S.D.	Δ
OC	55	Pre-treatment	2.13		± 0.56	
		After treatment	2.20		± 0.56	
		Difference	0.07	n.s.		
OC + smoke	30	Pre-treatment	2.33		± 0.71	
		After treatment	2.67		± 1.50	−0.47 *
		Difference	0.34	n.s.		
OC + alcohol	25	Pre-treatment	1.91		± 0.55	
		After treatment	2.03		± 0.66	+0.17 n.s.**
		Difference	0.12	n.s.		

OC: Group using low-dose oral contraceptives.
n.s.: Not statistically significant difference.
* : Statistically significant difference for $P \leq 0.05$.
** : Statistically significant difference for $P \leq 0.01$.
Δ : Difference vis-à-vis OC group.

RESULTS

Table 1 summarizes our results.

The mean AFP level was 2.13 ± 0.56 ng % ml in group 1 (OC), increasing to 2.20 ± 0.66 after treatment with oral contraceptives. This difference is not statistically significant.

In group 2 (OC + smoke) the mean AFP level was 2.33 ± 0.171 before treatment and 2.67 ± 1.50 after estroprogestinic treatment. This difference is not stastically significant.

In group 3 (OC + alcohol) mean AFP was 1.91 ± 0.55 before treatment and 2.03 ± 0.68 after treatment. This difference is not statistically significant.

A comparison of the three groups showed a significant difference as for $P < 0.05$ between groups 2 and 1. In all cases, however, AFP levels were well below 25 ng % ml.

DISCUSSION

Our data show no difference between AFP levels before and after treatment with estroprogestinics in the three groups examined. On the other hand, in the group of smokers who used oral contraceptives, AFP levels were higher than in the other two groups with a significant difference as for $P < 0.05$.

However, these increased levels were always within normal limits and never reached 25 ng % ml; AFP exceeding this value is regarded as evidence of liver damage.

These data show therefore that the association of smoke and oral contraception can have unfavourable implications for the liver function.

Despite the small number of cases this element is worth further studying. Data obtained by Sizaret *et al.* ([14]), who studied an Indian community in Singapore, are similar to ours.

A study by Seppala ([15]), who used the immunodiffusion technique (less sensitive than RIA), showed no pathological change in AFP levels in estroprogestinics users.

Rodeck *et al.* ([16]) too, who used RIA, found no difference between 'pill' users and controls.

However none of these Authors reported the living habits of the patients they examined in their study, while these habits are known to be possible risk factors in themselves. We do not know

what exactly the increase in AFP plasma levels of oral contraceptives users means; possibly in these patients smoke has a direct or indirect negative influence on the liver function as is true of other metabolic parameters. Development of liver neoplasms, whether benign or malignant, is currently considered to be an unusual but potentially lethal risk associated with the use of oral contraceptives.

Early diagnosis of this pathology requires accurate screening by complex and expensive examinations like angiography, echotomography and computed axial tomography.

Conversely, AFP assays are relatively simple and unexpensive. That is why AFP plasma level assay should be the routine screening test to detect liver neoplasms in all oral contraceptive users. Whenever high levels are found, all the other complex and costly examinations should be carried out.

BIBLIOGRAPHY

1) Dalen E., Westerrholm B.: *Acta Med. Scand., 125*, 459, 1974.
2) Orellana-Alcade J. M., Dominiguez J. P.: *Lancet, 2*, 1278, 1966.
3) Christopherson W. M., Truman M. E.: *Lancet, 1*, 1076, 1976.
4) Davis M., Portman B., Searle M., Wright R., Williams R.: *Brit. Med. J., 4*, 496, 1975.
5) Edmonds H. A., Henderson B., Benton B.: *New Engl. J. Med., 294*, 470, 1976.
6) Klaskin G.: *Gastroenterology, 73*, 386, 1977.
7) Stariffer J. O., Hill R. B.: *Ann. Int. Med., 85*, 122, 1976.
8) Antoniades K., Campbell W. N., Hcksher R. H., Kessler W. B., Mac Carthy Y. G. E.: *J.A.M.A., 234*, 628, 1975.
9) Kanai K., Endo Y., Oda T., Kanekko Y.: *Ann. N. Y. Acad. Sci., 259*, 29, 1975.
10) Endo Y., Kanai K., Oda T., Mitamura K., Jino S., Suzuki H.: *Ann. N. Y. Acad. Sci., 259*, 234, 1975.
11) Sakamoto S., Yachi A., Auzai T., Wada T.: *Ann. N. Y. Acad. Sci., 259*, 253, 1975.
12) Sell S., Stillman D., Coghman N.: *Ann. J. Clin. Pathol., 66*, 847, 1976.
13) Takata K., Watanabe A., Kosaka K.: *Ann. N. Y. Acad. Sci., 259*, 80, 1975.
14) Sizaret P., Tuyins A., Martel N., Jouveuceaux A., Levin A., Ong Y. W., Rive J.: *Ann. N. Y. Acad. Sci., 259*, 136, 1975.
15) Seppala M.: *Int. J. Fertil., 18*, 206, 1973.
16) Rodeck C. H., Campbell S., Biswas S.: *Brit. J. Obst. Gyn., 83*, 24, 1976.