LIVER FUNCTION STUDIES WITH AN OESTROGEN-PROGESTOGEN INJECTABLE CONTRACEPTIVE

by

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Certain C 17 alkyl substituted testosterones have been shown to be capable of affecting the excretory function of the liver (Fross 1959, Petersen 1963, Cordon 1962, Shaw 1960, Kauup 1962, & Wilder. 1962).

High doses of natural oestrogens were found by Muller and Kappas (1964) to increase bromsulphthalein retention.

The effect of combined high dose oral contraceptives on liver function have been extensively studied and reviewed (Pincus, 1965, Mears 1965, Swyer 1966, Brill 1966, Robertsen 1967).

This communication presents our experience with the effect of Daladroxate(*), a long-acting oestrogen-progestogen combination given intramuscularly, on liver functions.

Repeated examinations including liver function studies were carried out on te 6th and 12th cycles.

The liver function profile consisted of the following :

I.—**Evaluation of bepto-cellular integrity** :

(*a*) S.G.O.T. and S.G.P.T.,

(*b*) Thymol turbidity.

(*) 150 mg. 16a-17a dihydroxyprogesterone acetophenide and 10 mg. estradiol enanthate in one ml. oily solution supplied by : The Squibb Institute for Medical Tesearch.

II.—Assessment of metabolic status :

(*a*) Total proteins

(*b*) A/ G/ratio.

III.—Assessment of heptic excretory functions :

(*a*) Alkaline phosphatase

(*b*) Serun Bilirubin

(*c*) B.S.P. retention 45 min. after intravenous administration of B.S.P. 5 mg./kg. of body weight.

RESULTS

TABLE I

Hepato-cellular Assessment Determinations

Determinations	Mean levels		
	Premedicational	6 months after med.	12 months after med.
S.G.O.T. (Karmen U.)*			
—Urban group	12.56	11.96	12.31
—Rural group	12.90	12.60	14.00
—All cases	12.70	12.23	12.57
S.G.P.T. (Karmen U.)*			
—Urban group	13.62	13.67	17.44
—Rural group	14.90	14.25	17.66
—All Cases	14.19	13.91	17.47
Thymol turbidity (Shank-Hogland U.)*			
—Urban broup	3.51	3.16	4.33
—Rural group	2.96	3.04	4.36
—All cases	3.24	3.11	4.34

* Normal ranges = S.G.O.T., 8—20 (Karmen U.)
S.G.P.T., 6—15 (Karmen U.)
Thymol turbidity, 4 units.

TABLE II

Metabolic AAssessment Determihations

Determinations	Premedicational	Mean levels 6 month after med.	12 months after med.
Total proteins* (mg/100 ml.)			
—Urban group	7.4	7.79	7.12
—Rural group	7.08	7.42	7.4
—All cases	7.25	7.64	7.16
Albumin/globulin* ratio			
—Urban group	1.70	1.76	1.9
—Rural group	1.82	1.76	1.56
—All cases	1.76	1.77	1.85

(*) Normal protein level 6—8 gm. per cent
A/R ratio : 1.5—3.

TABLE III

Hepatic Excretion Assessment Determinations

Determinations	Premedicational	Mean levels 6 months after med.	12 months after med.
Alkaline Phosphatase (U/100 ml.)*			
—Urbao group	9.32	8.39	10.06
—Rural group	7.7	7.9	11.33
—All cases	8.59	8.18	10.26
Bilirubin (mg/100 ml.)*			
—Urban group	0.40	0.37	0.38
—Rural group	0.55	0.43	0.43
—All cases	0.46	0.40	0.39
B.S.P. retension % *			
—Urban group	1.47	1.45	1.58
—Rural group	1.93	1.85	1.7
—All cases	1.68	1.60	1.60

(*) Normal ranges = Alkaline phosph., 3—13 U/100 ml.
Total Bilirubin, 0.2—0.8 mg./100 ml.
B.S.P. retension 4%.

DISCUSSION

The effect of high dose oral contraceotive was extensively studied. In a careful review Mears (1965) discussed the effect oforal contraceptives on Thymol turbidity, Cephalin Cholesterol flocculation, Serum Albumin, Bilirubin and the Transaminases (S.G.P.T. and S.B.O.T.). She concluded that any changes produced in such tests were transient in character and were of little significance. Eisalo et al. (1964) a, d Palva and Mustala (1964) working in Tinland reported alternations inliver function in Postmenopausal wopmen receiving high dose oral Oestrogen Progestogen coêbination. In their series liver functions were assessed by measuring the serum concentration of Glutamic-Pyruvic and Glutamic oxalacetic transaminases. Bakke (1965) failed to demonstrate such alternations in a large series of Post-menopausal women treated with oral contraceptives in the U.S.A. The reason for the difference in results between h Finnish and American workers is not clear, but it is possible that dietary factors may be at least partly responsible.

Swyer (1966) and others have emphasized that in patients in whom liver function was previously normal, medication by Progestogen-oestrogen mixtures does not appear to cause jaudice, hepatic necrosis or progressive liver diseases. On the other hand, in women with preexisting liver disease, there is some evidence suggesting that further impariment of hepatic function is liable to occur.

Garcia and Wallach (1968) reported their experience with Deladroxate in 234 women and concluded that the liver function of these recipients were not adversely affected by this Progestogen-oestrogen formulation administered once monthly.

In this study the oestrogen-progesten combination was studied on two, groups of participants one group are villagers comming from rural areas where bilharziasis is endemic and the second group of urban participant. On both groups a battery of test covering as much as possible of the various functions of the liver were carried out before andduring the third six and twelveth cycles.

The tests veryfing the hepato cellular integrity included S.G.O.T., S.G.P.T· and Thymol turbidity tests proved to fall within the normal range, except for a very insignificant increase in the S.G.O.T. and thymol turbidity on the 12th. month after medication in both the urban and rural groups.

As for the tests covering the metabolic assessment (total protein and A/G ratio) the results were within the normal range.

The third function examined was the exertory functions of the liver by estimating the alkaline phosphatase, bilburin level, and B.sp. retention. The results of these tests were as well strictly within the normal range.

The above results suggest that this cestrogen-progestogen formulation administered in this dosage does not adversely affect the various liver function whether the hepato cellular, metabolic of exercetory of participants even in rural areas where bilharziasis is endemic.

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