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SHORT COMMUNICATION

METABOLISM OF STEROIDS IN FLUOROSIS

I. OESTROGENS IN MALE URINE

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SUMMARY

Forty-five male patients suffering from chronic fluorine poisoning and fifteen normal men were investigated. The urinary excretion of oestrone, oestradiol-17β, oestriol and 16-epioestriol was studied. The results revealed a high content of oestrogens in urine. This is explained by a metabolic disorder in the liver.

FLUOROSIS is considered to be one of the most widely spread occupational diseases. Fluorine is a polyenzymatic toxic agent causing the damage of various organs. Bone lesions and lesions of digestive organs, especially of liver, are primarily observed. Liver plays an important role in the metabolism of various compounds, including steroids.

This paper presents some results of an investigation of the urinary excretion of oestrone, oestradiol-17β, oestriol and 16-epioestriol by male patients suffering from occupational fluorosis.

Forty-five workers (aged 31–50 years) from cryolite and aluminium works were under observation. Their work extended over periods of 8–31 years. Clinical diagnosis – chronic occupational fluorosis (I, II and III stages). The patients were divided into 2 groups:

Group A: 34 patients with liver damage demonstrated by clinical and biochemical data.

Group B: 11 patients without liver damage.

Control group: 15 normal men.

The excretion of oestrone (Oe_1), oestradiol-17β (Oe_2), oestriol (Oe_3) and 16-epioestriol (16-epiOe_3) was investigated using Brown's method[1] as modified by Nocke and Breuer[2]. The Kober color reaction was done according to the Bradshaw modification[3].

The following liver function tests were used: serum bilirubin content and urine urobilin determination, floculation tests, serum protein electrophoresis, hippuric acid test, galactose loading curve, cholesterol blood concentration, and other biochemical analyses where necessary. Fluorine content in urine was determined in all cases.

Oestrogen excretion data for the normal men are presented in Table 1. Oestrogen excretion data for groups A and B are presented in Table 2.

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Table 1. Oestrogen content (μg/24 hr) of normal male urine

Statistical data	Sum total	Oe_1	Oe_2	Oe_3	16-epiOe_3
Mean	13·54	3·09	1·05	9·46	0·72
S.E. ±	1·0	0·62	0·3	0·68	0·15

Sum total: $Oe_1 + Oe_2 + Oe_3$.
Oe_1 – Oestrone; Oe_2 – oestradiol-17β; Oe_3 – oestriol;
16-epiOe_3 – 16-epioestriol.
S.E. – standard error of the mean.

Table 2. Oestrogen excretion (μg/24 hr) in fluorosis patients with (group A) and without (group B) liver damage

Statistical data	Sum total	Oe_1	Oe_2	Oe_3	16-epiOe_3
Mean	33·30	9·9	3·09	20·25	1·67
S.E. ±	2·5	0·89	0·38	1·8	0·2
P	$< 0{\cdot}001$	$< 0{\cdot}001$	$< 0{\cdot}05$	$< 0{\cdot}05$	$< 0{\cdot}05$
Mean	22·50	5·10	2·74	12·83	1·14
S.E. ±	1·3	0·6	0·7	1·0	0·2
P_1	$< 0{\cdot}05$	$< 0{\cdot}002$	$> 0{\cdot}1$	$< 0{\cdot}002$	$= 0{\cdot}1$
P_2	$< 0{\cdot}05$	$= 0{\cdot}05$	$0{\cdot}1 > P > 0{\cdot}05$	$= 0{\cdot}02$	$> 0{\cdot}1$

P_1 – probability between groups A and B.
P_2 – probability between control and B groups.
P – probability between control group and group A.

Group A. As is seen from Table 2, the oestrogen excretion in this group is elevated. Three patients of this group showed a very high oestrogen content in urine, especially of oestrone and oestriol (20·1 and 44·8; 19·8 and 28·3; 18·9 and 24·8 μg/24 hr, respectively).

The biochemical data for group A were as follows: serum bilirubin content (total 0·9–2·5 mg per 100 ml, conjugated 0·2–0·7 mg per 100 ml), urobiline in urine 4·2–11·0 mg per 1 litre, Weltmann coagulation band 8–10 test tubes.

Group B. The oestrogen excretion levels in this group were also elevated as compared with control group. The differences in oestrogen excretion in the urine between groups A and B were statistically significant. The liver function tests were normal.

We do not know of any literature concerning oestrogen metabolism in fluorosis. The data presented in this paper show a marked disturbance of oestrogen metabolism in this occupational disease.

Probably, one of the reasons for this lies in liver damage. The role which the liver plays in oestrogen metabolism was first shown by Zondek[4] in 1934 and fully reviewed by Jailer[5], Breuer[7, 8], Adlercreutz[9], Diczfalusy and Lauritzen[6] and Diczfalusy[10].

A number of authors[11–15] have found high oestrogen excretion in urine to be due to liver lesion. In the metabolic investigations performed recently by Zumoff *et al.*[14] with oestradiol-17β-H^3 in patients suffering from liver cirrhosis,

elevated excretions of oestriol and 16α-hydroxyoestrone were established. The excretions of oestrone, oestradiol and 16-epi-oestriol were not changed, but the excretion of 2-methoxyoestrone and of 2-hydroxyoestrone were reduced. The authors concluded that in this disease the 2-hydroxylation process is decreased and a 16α-hydroxylation process is activated.

In our investigation we found increased excretion of oestrone, oestradiol and oestriol in the patients of group A. Elimination of 16-epi-oestriol in the urine was also elevated but the oestriol/16-epi-oestriol ratio was not changed as compared with control group. In the patients of group B the excretion of oestrodiol and 16-epi-oestriol was statistically insignificant as compared with the results of the control group, but the excretion of oestrone and oestriol was statistically significant. This difference in the oestrogen excretion between our results and those of Zumoff *et al.* can be explained by the different pathological conditions (cirrhosis of the liver and toxic hepatitis respectively).

We did not perform any determinations of free oestrogens, as we are of Diczfalusy's opinion that a high amount of free oestrogen hardly denotes liver damage.

The high conjugation capacity of the intestinal wall may fully compensate the conjugation deficiency of the liver. As to the possible lesions of gonads, we shall deal with this problem in later communications.

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