TRYPTOPHAN AND THYROID METABOLISM IN TUBERCULOSIS

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Tryptophan, an essential amino acid, is biologically important as a precursor of serotonin and nicotinic acid derivatives[1].

The aim of this work is to study the metabolism of tryptophan in tuberculous patients at different stages of the disease before and after tryptophan load. A parallel study was also done in normal control subjects and tuberculous patients to study the hormonal pattern of thyroid gland in the different stages of tuberculosis and to exclude the effect of thyroid hormone as one of the causative agents for tissue destruction occuring in tuberculous patients.

MATERIAL AND METHODS

Fifty persons of both sexes and of different age were studied. These cases were classified as follows :

1) Ten normal healthy individuals as control group.

2) Thirty patients suffering from pulmonary tuberculosis, classified according to the classification of the National Tuberculous Association of America into :

   a) Ten cases with minimal lesion (Stage I).

   b) Ten cases with moderately advanced lesion (Stage II).

   c) Ten cases with far advanced lesion (Stage III).

3) Ten cases of quiescent pulmonary tuberculosis.

Blood samples were collected at fasting, 1, 2 and 4 hours after a loading dose of L-tryptophan (50mg/kg body weight).

For each sample we estimated :

—Serum total indoles by the method of Opienska et al[2].

Table 1. Serum Levels of Total Indoles, T_3, T_4 and TSH before and after Tryptophan Load

		Fasting				1 hour after load				2 hours after load				4 hours after load			
		Total indoles	T_3	T_4	TSH	Total indoles	T_3	T_4	TSH	Total indoles	T_3	T_4	TSH	Total indoles	T_3	T_4	TSH
Nomal control	Mean	1.92	1.41	9.19	3.95	8.65	1.021	10.719	3.98	11.09	1.08	10.58	3.65	7.01	1.13	9.74	3.68
	SE±	0.14	0.28	1.11	0.20	1.17	1.18	1.27	0.15	1.65	0.16	0.75	0.16	0.96	0.17	0.86	0.15
Tuberculosis Stage I	Mean	2.03	1.15	9.97	3.88	8.51	0.98	9.07	3.73	10.74	0.93	11.22	3.81	7.37	1.14	9.76	3.21
	SE±	0.10	0.12	0.44	0.14	0.38	0.16	0.88	0.19	0.85	0.08	1.37	0.10	0.67	0.33	0.74	0.10
	P	<0.5	<0.4	<0.5	<0.3	<0.4	<0.5	<0.4	<0.3	<0.5	<0.4	<0.5	<0.4	<0.5	<0.5	<0.5	<0.2
Stage II	Mean	2.71	1.14	11.27	3.83	8.96	1.13	10.72	3.76	11.23	1.30	9.92	3.75	7.74	1.08	10.62	3.83
	SE±	0.03	0.12	0.86	0.19	0.61	0.13	1.51	0.10	0.71	0.14	1.15	0.13	0.56	0.11	0.98	0.10
	P	<0.001	<0.5	<0.2	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.5	<0.4	<0.5	<0.5	<0.5	<0.5	<0.5
Stage III	Mean	3.48	1.21	10.72	3.75	11.06	1.11	10.43	3.75	14.87	1.00	10.66	3.83	10.11	1.17	10.32	3.83
	SE±	0.97	0.15	0.59	0.13	1.14	0.23	0.38	0.11	1.58	0.13	0.50	0.10	1.36	0.21	0.47	0.19
	P	<0.001	<0.5	<0.4	<0.5	<0.005	<0.5	<0.05	<0.5	<0.05	<0.5	<0.1	<0.5	<0.02	<0.5	<0.02	<0.5
Quiscent Tubercu-losis	Mean	2.06	1.21	9.87	3.83	6.58	1.18	8.63	3.76	8.51	1.06	9.32	3.8	6.42	1.02	8.87	3.75
	SE±	0.12	0.11	0.88	0.13	0.91	0.25	0.80	0.10	1.13	0.11	0.60	0.10	0.72	0.10	0.30	0.16
	P	<0.5	<0.5	<0.5	<0.5	<0.4	<0.5	<0.2	<0.2	<0.2	<0.5	<0.2	<0.5	<0.5	<0.5	<0.4	<0.5

P : is the statistical relation between each group and the normal control group.

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—Serum thyroxine (T_3), tri-iodothyronine (T_4) and thyroid-stimulating hormone (TSH) by radioimmunoassay.

Results

Results obtained are summarised in table 1.

The level of serum total indoles in tuberculous patients tended to increase. The elevation of their value were significant in stage II and III compared to normal control, stage I and quiescent pulmonary tuberculous patients.

The level of serum T_3 showed no significant change between different groups studied and also no significant change between fasting and after loading dose of L-tryptophan.

The level of serum T_4 showed no significant changes between different groups studied and also no significant changes between fasting and after loading dose of tryptophan.

The level of serum TSH showed no significant changes between different groups studied and also no significant changes between fasting and after loading dose of tryptophan.

Discussion

The fasting level of total indoles in normal adult humans appears to be rather constant. This constant level was regulated through homeostatic processes, being controlled by the liver, enzymes, vitamins and hormones[3)~5)]. Serum total indoles arise from absorption, synthesis and tissue catabolism represent a source that can be drawn upon during protein metabolism.

The increase in total indole derivatives during the disease, especially during its last stage might be due to increased destruction of lung tissue proteins and their further hydrolysis into amino acids including tryptophan. Another possibility is the hormonal unbalance which affects particularly nitrogen metabolism. Suprarenal cortical insufficiency was recorded in late stages of pulmonary tuberculosis[6)7)].

Abdel-Kader et al[8)]found a persisting hypoglycaemia in tuberculous patients after glucose tolerance test which was attributed to the insulin overactivity. This would evoke tryptophan release from the liver and affect its increase in blood. The level of serum total indoles in tuberculous diabetics was highly significantly lower than in tuberculous non-diabetic patients having the same extent of tuberculosis.

Abdel-Kader et al[9)]found that the amino acids tryptophan and histidine to be bacteriostatic for the *Mycobacterium tuberculosis*. In (1960), Abdel-Kader et al[10)], carried out further experiments on indole and skatole which proved to be bacteriostatic both *in vitro* and *in vivo* on guinea pigs. Indole and skatole showed some toxic effects on the liver, spleen and kidneys which limited their experiments.

The thyroid gland is not involved, comparable to the adrenal cortex and medulla, in the acute response to stress. The hypothalmic-pitiutary thyroid system seems to provide a constant supply of thyroid hormones, in spite of marked alteration in the external and internal milieur.

Thyroid gland activity is regulated by a negative feedback control system involving the pituitary and possibly the hypothalamus through the thyrotrophic releasing hormone. Increased production of TSH accelerates activity of the thyroid including production of T_3 and T_4 until blood hormone level returns to the control level[11)].

In this work T_3, T_4 and TSH pattern was studied in the different stages of tuberculosis and also in the normal control group. There was no significant difference between the serum T_3 level in the different stages of tuberculosis when compared to the normal control group. There was no significant change in the serum T_4 and TSH level in the 4 groups of patients studied when compared to the normal control group.

Also, there was no significant change in T_3, T_4 and TSH level after the tryptophan load, both in tuberculous patients and in the normal control subjects.

This finding exclude the hypothesis of hormonal inbalance in those tuberculous patients i.e. the thyroid hormonal affection as a destructive cause for lung tissue in these patients.

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