原　著

ADENOHYPOPHYSEAL ACTIVITY IN RELATION TO SUPRARENAL FUNCTION IN TUBERCULOSIS

Abdel Rahman A. Hafiez, Bothaina El-Kamma, Mohamed A. Abdel-Hafez* and Essam El-Nady

Biochemistry Department

Mahmoud A. Abdou, Abdel-Hakim M. Abdel-Hakim and Shaaban M. Ramadan

Chest Department, Kasr El-Aini, Faculty of Medicine

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This work was carried out on 150 subjects. They were classified into four groups : group I : Bronchogenic pulmonary T. B. (n=96) ; group II : Haematogenous T. B. (n=15) ; group III : Healed T. B. (n=16), group IV : Healthy control (n=23). Insulin tolerance test was done for each subject to assess the hypothalamo-hypophyseal axis. Glucose, ACTH, cortisol, GH, and PRL levels were estimated during fasting and over three hours after insulin administration. In group I and II the patients exhibited higher fasting levels of anti-insulin hormones and they respond greater than normals to insulin-induced hypoglycaemia. This might indicate early affection of the pituitary gland by TB infection, yet insulin-induced hypoglycaemia assured efficient function of the gland. In healed TB patients, no significant changes were obtained in the different hormonal behaviour, whether in the fasting state or after stimulation. This might be explained by improvement of the health condition of the patients, and relief of the stress induced by TB infection.

Key words : Bronchogenic tuberculosis, Haematogenous tuberculosis, Healed tuberculous patients, Growth hormone, Prolactin, Cortisol, ACTH, Insulin tolerance test

INTRODUCTION

Many investigators have reported the effects of various stressful stimuli on the release of pituitary gland hormones (1), (2), (3).

Tuberculosis, being a chronic destructive and stressful disease with a long-time relationship between the patient and the organism may impinge upon various body systems including the endocrine glands. The aim of this study is to

* Medical Biochemistry Dept., Faculty of Medicine, Cairo University, Kasr El-Aini, Cairo EGYPT.

elicit such interactions that are postulated to occur between tuberculosis as a stressful stimulus and some pituitary hormones.

MATERIAL AND METHODS

Tuberculous patients included in this study were 127 classified as follows : group I : Pulmonary TB patients (n=96) ; group II : Haematogenous TB patients (n=15) ; group III : Healed TB subjects (n=16).

Besides, control subjects were selected from the healthy hospital working staff and who gave no family history of TB and they were included as group IV (n=23).

The tuberculous patients were selected from in-patients of Chest Diseases Department in Kasr El-Aini Hospital. All patients were under treatment with different regimens of antituberculous drugs. The following investigations were done for each subject : sputum analysis for acid-fast bacilli, tuberculin test, chest roentgenogram, erythrocyte sedimentation rate and full blood picture.

According to the site and extent of tuberculous lesion (4), group I was subclassified into Grade I (minimal), Grade II (moderate) and Grade III (far-advanced lesions).

Sampling :

Insulin tolerance test was performed at 8.00 a. m. All subjects were overnight fast and they were maintained in bed during the period of the test. For the female subjects, the test was performed in the luteal phase of their menstrual cycles.

Venous blood samples were obtained with slight cuff pressure. After taking the fasting sample, the subject was injected intravenously by 0.1 U/kg body weight of soluble insulin.

Then blood samples were taken after exactly 5, 30 and 60 minutes from the end of insulin injection (5).

Serum samples were kept frozen (at −20°C) till estimation of growth hormone (6), prolactin (7), cortisol (8) and adrenocorticotropic hormone (ACTH) (9) by radioimmunoassay technique.

RESULTS

Basal serum glucose, ACTH, GH and PRL were insignificantly changed in Grade I patients whereas serum cortisol was significantly elevated compared to the healthy control group. Insulin induced hypoglycaemia caused variable significant elevation of cortisol, GH and PRL but unaltered glucose and ACTH levels in grade I subgroup compared with the control group. Grades II and III subgroups showed elevation of

Table 1. Serum levels of glucose (mg/dl), ACTH (pg/ml), cortisol (μg/dl) growth hormone (ng/ml), and prolactin (ng/ml) during insulin-induced hypoglycaemia test in normal and bronchogenic TB groups.

Group	Parameter	Glucose			ACTH			Cortisol			Growth hormone			Prolactin		
		"0" min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min
Normal n=28	Mean	83	54	70	160	226	203	10.4	19.0	20.1	1.3	3.4	6.3	8.1	15.5	23.5
	SE	2.17	1.66	2.12	4.77	10.11	8.83	0.58	0.93	1.26	0.18	0.42	0.53	1.8	1.55	2.56
Grade I n=23	Mean	86	52	68	153	240	202	13.8	24.9	23	1.0	2.0	3.1	0.7	11.3	16.6
	SE	1.66	1.69	1.68	12.04	14.56	15.82	0.2	1.35	1.55	0.11	0.19	0.38	0.6	1.19	1.77
	P_1	NS	NS	NS	NS	NS	NS	<0.001	<0.001	NS	NS	<0.005	<0.001	NS	<0.05	<0.05
Grade II n=36	Mean	92	59	71	190	268	260	16.8	29	27	1.5	2.6	3.6	9.3	16.5	22.1
	SE	1.09	1.21	2.00	5.09	5.77	8.8	0.68	1.26	1.37	0.13	0.27	0.4	0.59	0.71	1.05
	P_1	<0.001	0.02	NS	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	NS	NS	<0.001	NS	NS	NS
	P_2	<0.005	<0.005	NS	<0.01	NS	<0.005	<0.001	<0.05	NS	<0.002	NS	NS	<0.005	<0.001	<0.01
Grade III n=37	Mean	99	65	75	242	322	310	21	36.6	34.6	2.2	6.3	8.0	12.7	24.8	29
	SE	1.18	1.42	1.23	8.56	10.15	11.53	1.07	1.17	1.17	0.22	0.78	0.89	1.07	1.64	1.84
	P_1	<0.001	<0.001	<0.05	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.005	<0.005	NS	<0.05	<0.001	NS
	P_2	<0.001	<0.001	<0.005	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.01
	P_3	<0.001	<0.005	NS	<0.001	<0.001	<0.005	<0.005	<0.005	<0.001	<0.01	<0.001	<0.001	<0.001	<0.001	<0.005

Table 2. Serum levels of glucose (mg/dl), ACTH (pg/ml), cortisol (ug/dl) growth hormone (ng/ml), and prolactin (ng/ml) during insulin-induced hypoglycaemia test in normal, naemacogenous TB, and healed TB groups.

Group	Parameter	Glucose			ACTH			Cortisol			Growth hormone			Prolactin		
		0 min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min	0 min	30 min	60 min
Normal n=28	Mean	83	54	70	160	226	203	10.4	19.00	20.1	1.3	3.4	6.3	8.1	15.5	23.50
	SD	2.17	1.66	2.12	4.77	10.11	8.93	0.58	0.93	1.26	0.18	0.42	0.53	1.8	1.55	2.56
Haematogenous TB n=15	Mean	91	64	80	213	291	266	18.5	25.6	23.6	24	7.9	10	14.00	34.9	43.50
	SE	2.02	1.42	2.19	18.19	16.91	14.98	1.72	2.35	1.96	0.41	1.08	0.72	1.14	2.16	2.51
	P	<0.01	<0.001	<0.005	<0.01	<0.005	<0.001	<0.001	<0.02	NS	<0.02	<0.001	<0.001	<0.001	<0.001	<0.01
Healed TB n=16	Mean	85	53	74	147	232	215	14.1	21.1	20.5	1.7	7.9	8.8	10.0	29.5	37.0
	SE	1.73	1.94	1.4	12.91	18.03	10.85	0.76	1.41	1.72	0.21	1.19	0.83	1.14	3.67	2.76
	P	NS	NS	NS	NS	NS	NS	<0.001	NS	NS	NS	<0.001	<0.02	NS	<0.005	<0.001

serum glucose, ACTH, cortisol, GH and PRL levels in the tested samples versus that of the control. Both of these subgroups had elevated levels of those parameters compared to grade I subgroup. Also, grade Ⅲ subgroup had elevated levels of glucose, ACTH, cortisol, GH and PRL vs grade Ⅱ subgroup in the evaluated samples (Table 1).

Haematogenous TB groups had significantly increased levels of glucose, ACTH, cortisol, GH and PRL, in both basal and insulin-induced hypoglycaemia samples compared to the control group. These results are comparable with that of grade Ⅲ subgroup of group I. Healed TB groups results are matched with that of the healthy control group (Table 2).

DISCUSSION

Previous work from the Chest and Biochemistry Departments (Kasr El-Aini) described some metabolic disturbances in carbohydrate metabolism (10), and (11).The authors assumed that TB may predispose to diabetes mellitus. The mechanism(s) involved in this phenomenon were not clear. Glucose hypotolerance was present in advanced cases of TB while mild or moderate cases are glucose normotolerants (12). Further, this investigator demonstrated that the insulin curve during oral glucose load test showed a statistically significant lower insulin levels than the controls. These results stimulated our interest to evaluate the status of some hormones which are related to the glycaemia in TB patients. The literature of such studies are scanty.

The data obtained confirmed the previously described changes in fasting glucose levels (12). A significantly higher fasting glucose levels was observed in moderately and far-advanced TB patients. In TB patients with minimal lesions, the change in the fasting serum glucose was insignificant and was associated with insignificant change in GH, ACTH and PRL levels in the fasting state.

The elevation in the fasting blood sugar levels in the moderately and far advanced groups goes in parallel with the increased in anti-insulin hormones measured, i.e. the concentration of GH, ACTH, cortisol and PRL in the aumillieux, GH is known to have a hyperglycaemic effect probably by decreasing glucose utiliation by the muscles and adipose tissue (13), (14). The hyperglycaemic effect of ACTH is probably mediated by producing cortisol (14). PRL has been accused to be a diabetogenic hormone (15), (16). Jarrett Ⅱ et al. (17) demonstrated that PRL reduces insulin binding to its receptors on adipocyte membranes.

Insulin tolerance test was described to assess the hypothalamohypophyseal axis. The stress induced by hypoglycemia is a potent stimulus for the secretion of ACTH, GH and PRL (18).

The hypoglycemic effect of insulin, showed insignificant changes in TB patients vs normal

controls. This finding would be explained by the suggestion that the sensitivity of tissues to insulin is not altered in these patients. As similar finding is recently described by Moaz (19) who reported no significant differences occurring in blood glucose levels during IVTTT * in tuberculous patients and controls.

* Intravenous Tolbutamide Tolerance Test.

If the subject is exposed to physiological, pathological or severe psychological stress (20) both ACTH and cortisol are elevated. Sustained stress results in prolonged high ACTH and cortisol levels (1) through reflex stimulation of the hypothalamic releasing factor.

The cortisol levels as well as the areas representing induced changes in blood cortisol during the test showed significant variations in the three subgroups of tuberculous patients vs normal controls. The cortisol levels rose progressively with the severity of the disease. This might be due to exaggerated response of the adrenal cortex to the circulating ACTH.

The results of this study showed that the peaks of GH levels in normals and tuberculous patients were after 60 minutes of insulin injection. In the tuberculous patients, these peaks were significantly lower than that of the healthy control group. This may suggest that the GH secreting cells have impaired sensitivity to hypoglycaemia or that the peak of GH after insulin is delayed later than 60 minutes, the time of the last sample obtained in this study. Fasting levels of GH in grades II and III vs group I showed significant increase. These two subgroups (moderate and far-advanced) had more destruction in the pulmonary tissues, with subsequent liberation of free amino acids. Abdel-Hafez (11) reported elevated levels of total free amino acid nitrogen in plasma of tuberculous patients, and this increase was proportionate with the severity of tuberculosis. Amino acids are potent stimulators for GH secretion.

Prolactin levels increased gradually during insulin tolerance test both in normals and tuberculous patients. The peak of PRL was always attained at 60 minutes. Similar results were reported by Woolf and Lee (21) in normal subjects. Psychic stress is also reported to stimulate prolactin secretion (3).

It was noteworthy to mention that fasting level of prolactin was lower than normals in mild TB infection. ACTH and GH behaved similarly in the same group which may point-out to initial supression affection of the pituitary gland in mild cases of TB. This is confirmed by the finding that the areas of response of PRL in this group is lower than in namely moderate and far advanced (22).

The changes in the different hormone levels measured in this study may indicate affection of the pituitary gland by TB infection.

In the healed patients, no significant change was noticed in the profile of the investigated hormones whether in the fasting state or after stimulation. This might be explained by the relief of stress induced by TB infection.

In the haematogenous tuberculosis the organ (s) are infected by the tubercle bacilli via the blood stream. ACTH levels in all samples are significantly higher than the corresponding levels in the normal controls. These results are similar to those obtained in the pulmonary group (bronchogenic). The other hormones behaved similarly.

One can conclude that in tuberculosis, bronchogenic or haematogenous, particularly in moderately or severely advanced cases, the patient exhibit high fasting levels of the anti-insulin hormones and they respond greater than normals to insulin-induced hypoglycaemia.

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