

Adrenal gland function and impaired glucose tolerance test in patients with pulmonary tuberculosis

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Tuberculosis is a cause of adrenal insufficiency. Impaired glucose tolerance (IGT) test has been observed very frequently in tuberculosis patients. To determine of relation between glucose intolerance and adrenal function, it was studied on newly diagnosed adult patients with pulmonary tuberculosis. While 18 patients had impaired glucose tolerance test, 37 patients had normal test. Adrenal functions were tested by using ACTH stimulation test. Basal and stimulated Cortisol levels were studied in all patients with abnormal glucose tolerance test, while only 22 of 37 patients with normal glucose tolerance could be studied for basal and stimulated Cortisol levels because of technical reasons. In each group, after ACTH stimulation, Cortisol levels were higher than basal Cortisol levels. But there were no significant difference between two groups for basal and after stimulation Cortisol levels, weight, height, body mass index (BMI), drug resistancy, duration of history and extention of diseases. However mean age of IG T group was higher than other group. We suggest that IG T is not related to adrenal gland function but to old age and infection in tuberculosis patients.

[Turk J Med Res 1995; 13(1): 21-24]

Key Words: Adrenal gland function, Pulmonary tuberculosis

Impaired glucose tolerance has been shown in some patients with pulmonary tuberculosis (1-3) and this has been attributed to the release of some hormones (ACTH, Cortisol, glucagon) in response to stress caused by tuberculosis infection (4). Also, with ACTH stimulation or dexamethasone suppression, significant changes in the levels of **Cortisol** have been found (5). In this study, basal and stimulated **Cortisol** levels have been investigated in pulmonary tuberculosis patients with and without abnormal glucose tolerance.

MATERIALS AND METHODS

The study included 55 newly diagnosed pulmonary tuberculosis patients with acid fast bacteria positive sputum. Chest films were taken in each patient. Extention of the disease in the chest films was classified as minimal, moderate and far advanced by using NTA (National Tuberculosis Association of USA) criteria (6). Mean age of the group was 32±0.4. None of the

patients had history of diabetes mellitus and fasting blood glucose levels were less than 140 mg/dl in all patients. Patients with malnutrition, gastrointestinal system disease, another concomitant infection, and patients who underwent surgical intervention or who were on medications that could influence glucose tolerance were excluded from the study. The diet of the patients contained at least 150 gr of carbohydrate per day and physical activity of the patients were not restricted. Blood samples for fasting glucose level were taken following 10 hours of fasting in the morning. After oral administration of 75 gr glucose, blood glucose levels were checked at 30, 60, 90, 120 minutes. The results were evaluated by using American Diabetes Association criteria. Impaired glucoses tolerance was found in 18 of 55 patients. Basal and stimulated **Cortisol** levels were studied in all patients with abnormal glucose tolerance could be studied for basal and stimulated **Cortisol** levels because of technical reasons. Basal **Cortisol** levels were measured in blood samples drawn at 8 a.m. and stimulated Cortisol levels were measured one hour after intramuscular injection of tetracosactrin (0.25 mg). Normal values for basal **Cortisol** were taken as 150-600 nmol/L. After stimulation with ACTH, an increase more than 300 nmol/L from baseline was accepted as positive, an increase between 200-300 nmol/L as

Received: Dec. 1,1994

Accepted: Dec. 21,1994

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suspicious and an increase less than 200 nmol/L as negative. Cortisol levels were determined by using standard RIA kit (Amerlex, Cortisol RIA kit). Measuring scale was 0-1700 nmol/L (0-60 microg/ml).

Statistical analysis was performed by using student's t Test chi-square test and Fisher's test.

RESULTS

Oral glucose tolerance test was found abnormal in 18 of 55 patients (32.7%). Mean age of patients with impaired glucose tolerance and normal glucose tolerance test was 38.7+0.2 and 29.8+0.3 respectively. There were no significant difference between two groups for weight, height, body mass index (BMI), drug resistance, duration of history and extension of diseases. Patient characteristics and chest film findings have been shown in Table 1 and 2. In the group with impaired glucose tolerance basal and stimulated Cortisol levels were 405.6+0.5 nmol/L and 614.4+0.5 nmol/L while in the group with normal glucose tolerance these values were 409+0.4 nmol/L and 654.4+0.5 nmol/L respectively. In each groups, the difference in basal and stimulated **Cortisol** levels were statistically significant ($p < 0.05$). There was no statistically significant difference between two groups in basal and stimulated Cortisol levels ($p > 0.05$) (Table 3). In impaired glucose tolerance group, the response to ACTH stimulation was found positive in 4 cases suspicious in 4 cases and negative in 9 cases, while normal

Table 1. Patient characteristics

	Normal GT	Impaired GT (1)
Age	29.8+0.3	38.7+0.2* (t=3.18)
Height	169.5+0.4 cm	168.0+0.1 cm" (t=1.96)
Body Weight	61.1+0.8 kg	59.1+0.2 kg" (t=1.95)
Body Mass Index	0.36	0.35" (t=1.95)
Duration of disease		
0-6 mo.	15	14"
over 6 mo.	7	14
Drug Resistance		
Yes	7	6"
No	15	12

* $p < 0.05$ " $p > 0.05$
(1): GT: Glucose tolerance test

Table 2. Classification of the disease on the chest radiographs

Classification	Normal GT	Impaired GT (1)
Minimal	4	2
Moderately advanced	14	11
Far advanced	5	4

" $p > 0.05$ (Fisher's exact chi-square)
(1): GT: Glucose tolerance test

Table 3. Cortisol levels of patients

	Normal GT	Impaired GT (1)
Basal Cortisol		
Levels (nmol/L)	409.0+0.4	405.6+0.5" (t=1.96)
After Stimulation		
Cortisol levels (nmol/L)	654.4+0.5	614.4+0.6" (t= 1.98)

" $p > 0.05$
(1): GT: Glucose tolerance test

Table 4. Responses to ACTH stimulation

Response	Normal GT	Impaired GT (1)
Positive	9	4"
Negative	9	10"
Suspicious	4	4"

" $p > 0.05$ (Fisher's exact chi-square)
(1): GT: Glucose tolerance test

glucose tolerance group had 9 positive, 4 suspicious, and 9 negative responses. Cortisol response to ACTH stimulation between the two groups was not statistically significant ($p > 0.05$) (Table 4).

DISCUSSION

The relationship between active pulmonary tuberculosis and impaired glucose tolerance has been noticed for long time with a reported incidence of 8.8% to 41% in different studies (1-3,7,8). In our study the incidence of abnormal glucose tolerance was found 32.7%. It has been proposed that abnormal glucose tolerance is a result of increased levels of anti-insulin hormones released as acute phase reactants in response to the infectious process caused by tuberculosis and it would improve with the treatment of infection (4). In one study there was no statistically significant difference in impaired glucose tolerance between tuberculosis and non-tuberculosis infection patients (7).

The tetracosactrin stimulation test is used to examine the secretory potential of the adrenal cortex. A wide variety of methods are available for ACTH stimulation test (9-11). We adapted the test which was developed by Wood JB. Wood et al showed that the initial plasma Cortisol response to a single intramuscular injection of 0.25 mg tetracosactrin was similar to the maximal response to porcine corticotropine given by intravenous infusion (9). The intramuscular tetracosactrin test was found to be reasonably reproducible and accurate (5,9,12).

Adrenal cortical function has been investigated in a number of studies. Barnes et al (13) have found elevated **Cortisol** levels in 39% and insufficient response to ACTH stimulation in 8% of the cases. In another study, insufficient response to ACTH stimula-

tion has been shown in 55% of African tuberculosis patients (12). In one study there was no statistically significant difference in adrenal cortical function between tuberculosis and non-tuberculosis patients (14).

Shrivastava et al (16) demonstrated that newly diagnosed tuberculosis patients had higher plasma **Cortisol** levels than normal subjects and this was inversely correlated with the duration of the disease. Sarma et al (5) found elevated levels of Cortisol in tuberculosis patients compared to normal subjects, but response to ACTH stimulation was higher in normal subjects compared to tuberculosis patients (5).

In our study, adrenal insufficiency was found totally in 19 cases (48%). Negative adrenal response to ACTH stimulation between 8% and 55% in other studies (12,13). These different results may be due to extension, severity and duration of the disease. Ellis et al observed that insufficient adrenal response decreased with anti-tuberculosis treatment. Our patients also had no treatment before and during ACTH stimulation. Tuberculosis is a cause of adrenal failure (13). In developed countries tuberculosis incidence has declined. So its importance in the etiology of adrenal failure has diminished. But tuberculosis is still a serious problem in our country (15) and we can expect high rate of adrenal insufficiency in tuberculosis patients.

In this study adrenal function was investigated between two groups of pulmonary tuberculosis patients with normal and abnormal glucose tolerance. The two groups were not different in regard to body weight, height, duration and extension of disease (Table 1-2). We did not find any difference in basal **Cortisol** levels between two groups (Table 3) ($p>0.05$).

After stimulation with ACTH, **Cortisol** levels increased in both groups significantly. In normal glucose tolerance group this increase was more prominent but the comparison of the two groups revealed no significant difference (Table 3) ($p>0.05$). In some studies, **Cortisol** response to ACTH stimulation has been reported to be lower in patients with tuberculosis compared to normal people (5,12) while in some other studies no difference has been found (13,14,17). The differences in these results may be due to different patient groups differences in extent of disease and in treatment in various studies.

Mean age of abnormal glucose tolerance group was higher than normal glucose tolerance group ($p<0.05$). Age is a known factor affecting glucose tolerance (17).

We conclude that impaired glucose tolerance is a frequent finding in patients with pulmonary tuberculosis but there is no clear relationship between abnormal glucose tolerance and basal or stimulated **Cortisol** levels. Impaired glucose tolerance in patients with pulmonary tuberculosis may be due to an acute phase reaction to infection and also may be related to other factors such as age.

Turk J Med Res 1995; 13(1)

OGTT bozuk akciğer tüberkülozlu hastalarda adrenal bez fonksiyonları

Tüberküloz adrenal yetmezliğin bir nedenidir. Oral glukoz tolerans test (OG TT) bozukluğu tüberkülozlu hastalarda yüksek oranda izlenmektedir. OGTT bozukluğu ve adrenal bez fonksiyonu arasındaki ilişkiyi incelemek amacı ile yeni tanı konmuş 55 erişkin akciğer tüberkülozlu hasta üzerinde çalışıldı. 18 olguda glukoz tolerans testi bozuk bulunurken 37 olguda normaldi. Teknik nedenlerden dolayı 37 normal OGTT'li hastanın 22'sinde bozuk OGTT'li hastaların ise hepsinde ACTH stimülasyon testi ile adrenal fonksiyonlar araştırıldı. ACTH uyarımı sonrası kortizol düzeyleri her iki grupta bazal düzeyden anlamlı olarak yüksek bulundu. Ancak gruplar arasında anlamlı fark yoktu. Boy, vücut ağırlığı, vücut kitle indeksi (BMI), ilaç direnci, hastalık süresi ve yaygınlık açısından da iki grup arasında fark izlenmedi. Ancak glukoz tolerans testi yüksek olan grupta yaş ortalaması diğer gruptan anlamlı yükseklik gösterdi. OGTT bozukluğunun adrenal bez fonksiyonları ile ilişkili olmadığı, ileri yaş ve enfeksiyon durumu ile ilgili olduğu sonucuna varıldı.

[Turk J Med Res 1995; 13(1): 21-24]

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