

English version: INFLUENCE CORTICOSTEROIDS ON THE FUNCTION OF THE ADRENAL CORTEX FOR PATIENTS WITH FIRSTLY DAIGNOSED DESTRUCTIVE PULMONARY TUBERCULOSIS*

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To study the effect of exogenous corticosteroids on adrenal function by tuberculosis the level of plasma cortisol and aldosterone in patients that were first diagnosed with destructive pulmonary tuberculosis, their correlation, and changes in the treatment process were defined. Before treatment in patients with destructive pulmonary tuberculosis diagnosed for the first time a significant increasing the cortisol level and decreasing aldosterone in plasma, compared with the data of the control group were observed. Addition of exogenous corticosteroids is not depressing, considering the daily biorhythm of adrenal function to the complex treatment of patients diagnosed with the destructive pulmonary tuberculosis for the first time, but has a modest stimulatory effect on the function of the adrenal cortex, wich results in slower normalization of cortisol level and a slight increase the level of aldosterone in plasma; thus promotes reducing terms and increasing the efficiency of treatment. The high level of mineralocorticoids (aldosterone) supports the anti-inflammatory potential of tissues, causing suppression of anti-inflammatory effect glucocorticoids, contributing to the increasing terms of treatment and reduction of its effectiveness and can be considered as an adverse prognostic factor, regarding prognosis and treatment of tuberculosis in these patients.

Key words: tuberculosis, the function of the adrenal glands, cortisol, aldosterone, treatment, corticosteroids

One of the most important factors of homeostasis support in the body under intoxication stress is the function of the adrenal cortex, which provides adaptive processes by biosynthesis of cortisol and aldosterone, which are factors of anti-inflammatory and anti-inflammatory potential of tissue forming characteristics of the pathological process. Glucocorticoids and mineral corticoids have oppositely direct effect. Glucocorticoids (cortisol) make anti-inflammatory effect, and mineral corticoids (aldosterone) potentiate the inflammatory process. If the glucocorticoid function of the adrenal tuberculosis was widely studied in 70-80 years of the last century [2, 3, 11, 13], so in general, their mineral corticoid functions were self without attention. There are only a few works, including in which was made determination the level of aldosterone [9, 11], corticosterone [2, 6] and several works in which estimated function of the renin-angiotensin-aldosterone system in tuberculosis [5, 8], but a complex study of both glucocorticoid and mineral corticoid function of adrenal tuberculosis wasn't conducted, although their study is essential in the correction the inflammatory potential of tissues during pathological processes, including, tuberculosis.

Determination of cortisol and aldosterone level in plasma of patients with tuberculosis and their correlation and study of the changes of level of these hormones with the influence of corticosteroid (CS) therapy may reveal mechanisms of sanogenesis during treatment of tuberculosis. The purpose of the work was to determine the level of plasma cortisol and aldosterone, their correlation in patients firstly diagnosed of destructive pulmonary tuberculosis, and studied their changes during treatment and with the influence of glucocorticosteroid drugs.

Materials and methods

The level of cortisol and aldosterone was determined in 38 patients with firstly diagnosed destructive pulmonary tuberculosis with excretion mycobacterium tuberculosis who were hospitalized in the Poltava Regional Clinical TB Dispensary. Depending on the mode of treatment,

all patients were divided into two groups. The group ATD+CS - 23 patients received standard anti-TB chemotherapy [7] with the additional purpose of the intensive phase of prednisolone given daily biorhythm of the adrenal function (20 mg every other day, in the morning, once, for at least 2 months, with removal of the drug once, without reducing pharmacotherapeutic dose) [1, 10, 12]. The ATD group – 15 patients received only anti-TB drugs (ATD) in standard mode. By sex, age, clinical forms and severity of tuberculosis process groups were identical. The control group consisted of 11 healthy volunteers. During the research, patients' rights were taken into account in accordance with the Helsinki Convention.

The hormonal researches were made at the Research Institute for Genetic and immunological grounds of pathology and pharmacogenetics of the Higher State Educational Establishment of Ukraine "Ukrainian Medical Stomatological Academy" in Poltava by modern standard kits (DRG ® Cortisol ELISA (EIA 1887) and DRG ® Aldosterone ELISA (EIA 4128), DRG International Inc., USA). Blood sampling for researches were made in the morning (7³⁰-8³⁰), on an empty stomach. In order to eliminate the influence of various factors on the results of research, they excluded medication for 5-7 days to the taking of blood that can affect for hormone level in blood, they were advised to keep mental calm, do not drink alcohol and do not abuse salty food. The hormone level was determined in patients on hospitalization (before treatment), in 2-3 months (after the intensive phase of treatment) and before discharge from the hospital.

Efficiency of treatment was determined by the dynamics of the clinical manifestations of the disease, normalization of hemogram, suspension of excretion mycobacterium tuberculosis, resorption focal and infiltrative changes or sealing and healing cavities. Statistical analysis of the results of researching was made with help of spreadsheets Microsoft Office Excel 2007 [4] with the definition of the average value of its average error and Student's t-

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test. The difference between the parameters that were studied was considered reliable at $p < 0,05$.

Results and discussions

Before treatment the patients with tuberculosis of both experimental groups showed a significant increase in the average level of cortisol ($244,41 \pm 7,77$ and $231,89 \pm 13,55$ ng / ml, $p > 0,05$, respectively) decreasing the average level of aldosterone ($93,0 \pm 4,34$ and $88,09 \pm 10,14$ pg/ml, $p > 0,05$) compared with the data of the control group (table 1). At the end of the intensive phase of treatment (after taking prednisone of sick people of the group ATD+CS) in both groups was marked decreasing the level in cortisol ($229,41 \pm 9,26$ and $200,89 \pm 12,69$ ng/ml, $p > 0,05$), more pronounced decreasing was the patients from the ATD group, that received only anti-TB drugs. This trend was observed at the end of treatment ($202,5 \pm 3,99$ and $194,13 \pm 8,87$ ng/ml, $p > 0,05$, respec-

tively). The aldosterone level increased after 2-3 months of treatment the patients from ATD+CS group ($109,46 \pm 5,98$ pg/ml), whereas it has not changed at the ATD group ($87,56 \pm 7,61$ pg/ml, $p < 0,05$). The patients from the ATD+CS group showed a significant decreasing of aldosterone at the end of treatment ($76,3 \pm 2,45$ pg/ml) and the patients from the ATD group was a significant increase its - ($112,25 \pm 4,97$ pg/ml, $p < 0,001$).

Identified trends are related to the fact that additional purpose of prednisone, given the daily biorhythm of the adrenal function, the patients from ATD+CS were made modest stimulatory effect at adrenal function without causing its depression, which manifested a moderate pace normalize cortisol level and a slight increase aldosterone levels after 2-3 months of treatment, in contrast to the indicators of ATD patients and led to increasing the efficiency of treatment the patients of ATD+CS group.

Table 1
The level of cortisol and aldosterone in plasma of TB patients before treatment and in the dynamics

Time	Control group (n=11)		Group ATD+CS (n=23)		Group ATD (n=15)	
	Cortisol, M±m, ng/ml	Aldosterone, M±m, pg/ml	Cortisol, M±m, ng/ml	Aldosterone, M±m, pg/ml	Cortisol, M±m, ng/ml	Aldosterone, M±m, pg/ml
Before treatment	161,98±23,92	117,87±10,85	244,41±7,77*#	93,0±4,34*#	231,89±13,55*#	88,09±10,14*
After 2-3 months of treatment			229,41±9,26*#	109,46±5,98*^	200,89±12,69	87,56±7,61*#
At discharge			202,5±3,99	76,3±2,45^#	194,13±8,87	112,25±4,97

Note: * - the difference is likely compared to the data at discharge within the group ($p < 0,05 - p < 0,001$);
^ - the difference is likely compared with the corresponding data of the ATD group ($p < 0,05 - p < 0,001$);
- The difference is likely to compared to the data of the control group ($p < 0,05 - p < 0,001$).

So, 86,96% of patients from the ATD+CS group, which additionally administered prednisone, after 2-3 months of treatment surcease excretion mycobacterium tuberculosis, 43,48% of patients - closed cavity decay, 47,83% of patients - dissolved or sealed the focal and infiltrative changes in the lungs and 69,57% of patients - normalized hemogram values. The results were worse: 46,67%, 20,0%, 26,67% and 33,33% respectively at the patients of ATD group, who received only chemotherapy.

Identified trends were the same at the end of treatment too. The patients from the ATD+CS group of the effectiveness of treatment achieved: surcease excretion mycobacterium tuberculosis - 91,33%, the closing of cavities - 73,91% resorption or sealing of the focal and infiltrative changes - 86,96%, the normalization of hemogram - 95,65% compared with patients of the ATD group (66,67%, 40,0%, 53,33%, 66,67%, respectively).

The high level of mineralocorticoids (aldosterone) was found from the patients ATD group at the end of treatment, supported pro-inflammatory potential of the tissues, causing suppression of anti-inflammatory the effect of glucocorticoids what influenced for the time of treatment and reduce its effectiveness. So, after 6 months of treatment, 60% (the average level of aldosterone $102,6 \pm 5,63$ pg/ml) of the patients of ATD group, who took only anti-TB drugs, has remained infiltrative changes in the

lungs, 73,3% (average aldosterone - $104,35 \pm 5,49$ pg/ml) - it has not closed the cavity of decay yet and 46,67% (the average level of aldosterone $121,04 \pm 5,69$ pg/ml) - were noted the hemogram changes. The received results are partially the same with the data of another author [7], who pointed out the increasing the level of aldosterone ($105,6 \pm 10,5$ pg/ml) the patients with tuberculosis that cavities close after 6 months of treatment, compared with those whom they healed during the first 6 months of treatment ($86,2 \pm 7,5$ pg/ml). The author didn't take into account the other indicators of the effectiveness of treatment.

The correlation of cortisol / aldosterone before treatment and in the dynamics of the patients in both groups is presented in the table 2, from which we can see that before treatment and after 2-3 months it did not differ significantly, but at the end of treatment the patients from the ATD group demonstrated a sharp decrease in the ratio of cortisol / aldosterone ($1,77 \pm 0,07$ pg/ml). In a detailed analysis of the characteristics of the disease in these patients it was found, that the majority of patients with the lowest ratio of cortisol to aldosterone maintained infiltrative changes in the lungs longer which promoted the lower effectiveness of treatment for patients who received only anti-TB drugs.

Table 2
The correlation of cortisol/aldosterone before treatment and in the dynamics, M±m

Groups	Before treatment	After 2-3 months of treatment	At discharge
Group ATD+CS (n=23)	2,87±0,13^	2,51±0,18^	2,8±0,05*^
Group ATD (n=15)	3,15±0,25*^	2,56±0,2*^	1,77±0,07
Control group (n=11)		1,42±0,13	

Note: * - the difference is likely compared to the data at discharge of the ATD group ($p < 0,001$);

^ - the difference is likely compared to the data of the control group ($p < 0,05 - p < 0,001$).

Conclusions

1. Before treatment in patients with firstly diagnosed destructive pulmonary tuberculosis with excretion mycobacterium tuberculosis a significant increasing the cortisol level and decreasing aldosterone in plasma, compared with the data of the control group. were observed

2. Addition of exogenous corticosteroids is not depressing, considering the daily biorhythm of adrenal function to the complex treatment of patients with firstly diagnosed destructive pulmonary tuberculosis, but has a modest stimulatory effect on the function of the adrenal cortex, wich results in slower normalization of cortisol level and a slight increase the level of aldosterone in plasma; thus promotes reducing terms and increasing the efficiency of treatment.

3. The high level of mineralocorticoids (aldosterone) supports the anti-inflammatory potential of tissues, causing suppression of anti-inflammatory effect glucocorticoids, contributing to the increasing terms of treatment and reduces its effectiveness and can be considered as an adverse prognostic factor, regarding prognosis and treatment of tuberculosis in these patients.

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