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THE ROLE OF SERUM NEOPTERIN LEVEL IN THE MONITORING OF TREATMENT FOR PULMONARY TUBERCULOSIS

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Резюме: Изучение уровней неоптерина у больных туберкулезом легких с разным эффектом терапии показало достоверное поэтапное снижение при эффективном лечении и стабильные показатели при замедленном и отрицательном эффекте. Эти тенденции позволяют рекомендовать неоптерин, как мониторингофвый показатель эффективности лечения при туберкулезе .

Resume: The study of neopterin levels in patients with pulmonary tuberculosis with different effects of treatment showed: a reliable consistent decriasing in effective treatment and stable indicators in a delayed and negative effect. These trends allow to recommend neopterin, as a monitoring indicator of the efficasy of treatment for tuberculosis.

Neopterin (2-amino-4-hydroxy6-pteridine) is an indicator of cell-mediated immunity. This biomarker is synthesized by activated monocytes, macrophages and dendritic cells that are stimulated by gamma-interferon produced by T-lymphocytes [1, 5]. In Tuberculosis (TB) science neopterin is considered as a diagnostic marker of this disease, as an indicator of the activation of TB from the latent form and as an indicator for monitoring the effectiveness of anti-TB therapy.

Literature review shows that the study of the dynamics of the content of neopterin in patients with different treatment effects has not been performed before, and therefore its role in monitoring of the treatment efficasy for pulmonary tuberculosis remains unclear [2, 3, 4, 5].

The purpose: to determine the dynamic of serum neopterin levels in patients with positive and delayed or/and negative effects on treatment with standart anti-TB treatment regimens, to determine the role of neopterin as a monitoring indicator of treatment efficacy.

Tasks: 1) to determine the levels of serum neopterin in groups of TB patients and practically healthy persons;

2) to compare the dynamic of the levels of serum neopterin in between groups of TB patients and with practically healthy persons;

3) to determine the most informative stage of serum neopterin measurement for monitoring of the efficasy of treatment for TB.

Materials and methods: 80 patients with pulmonary TB were included in the study. 1 group – 30 patients with positive effect to the anti-TB treatment, that had convertion of bacteriaexcrection after 60 doses of therapy; 2 group – 50 patiens with delayed or/and negative effects on treatment, that had convertion of bacteriaexcrection after 90-120 doses of therapy (subgroup A - 30 patients) or had a persistant bacteriaexcrection, negative radiological and clinical dynamic and got a result of treatment “Failure” after 120 doses (subgroup B - 20 patients). The control group consisted of 20 practically healthy persons. The diagnostic samples were carried out in 3 stages: 1 - at the beginning of anti-TB treatment; 2 - after 60 doses for the first group, after 90-120 doses for the second group; 3 -

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for the first group and the subgroup A at the end of anti-TB treatment, for the subgroup B with determined of the result of "Failure".

The content of neopterin in blood serum was determined by ELISA method with using of the Awareness Technology Stat Fax 303 Plus Microstrip Reader (USA) and standard set of Neopterin-96 reagents manufactured by IBL (Germany). Mann-Whitney criterior was used, while significant differences were considered as such at $p<0,05$. Statistical data processing was performed using Statistica 6.1 software (StatSoft).

Results and discussions: The dynamic of serum neopterin levels in the group of TB patients with positive effect to the anti-TB treatment and in the group with delayed or/and negative effects on treatment, compared with practically healthy persons is presented in the Table 1. Significant ($p<0,05$) increase of neopterin was determined at the 1 monitoring stage in both groups of TB patients, in comparison with the control group. Neopterin was higher to 47,5 % and 53,2 %, in first and second group, respectively. At the 2 monitoring stage neopterin level were significant ($p<0,05$) decrease on 25,5% in the first group, in the second group there is no any dynamics. At the 3 monitoring stage in the first group the levels of biomarker approached the norm and did not differ from the control. In subgroup A levels of all indicators were higher then in first group, as in sugroup B.

Tab. 1 The dynamic of serum neopterin levels in the group of TB patients with positive effect to the anti-TB treatment and in the group delayed or/and negative effects on treatment, compared with practically healthy persons.

Monitoring stages		1 stage		2 stage		3 stage	
group	Control	1	2	1	2	1	2
Neopterin (nmol/l)	5,56 ±2,079	11,71 ±2,476*	10,44 ±1,43*	8,72 ±1,62	10,57 ±2,18	4,4 ±1,41#	12,56 ±2,43#

* - significantly ($p <0.05$) is assigned with control group.
\# - significantly ($p <0.05$) is assigned between groups in the same stage.

Conclusions: Positive effect of anti-TB therapy is accompanied by decreasing of neopterin. Delayed effect, when bacterial excretion persists and there is a negative clinical and radiological dynamics more than after 2 months of therapy, cell immunity parameters are stable. Patients with the result of "Failure" noted a steady increase in neopterin levels. The indicated trends provide an opportunity to propose the study of the dynamics of the content of neopterin, as a marker for monitoring treatment efficasy and early prediction of its failure. The most informative is measurement of serum neopterin for monitoring of the efficasy of treatment for TB in the bigining of treatment and after 60-90 doses.

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