Results: The genotypes frequency for TNF-α, IL-4, and IL-4Rα were equally distributed in the patient group in comparison with the controls. However, there were significant differences for IL-4 C-590T gene between the subgroups of asthmatics with different degree of the disease severity. Thus, *IL-4* CT+TT at position -590 was significantly overrepresented in children with severe asthma in comparison with those with the moderate one (53,8% in severe asthma vs 25,0% in moderate asthma; χ^2=2,7; gl=1; p=0,086). The same difference was found for the T allele (minor allele): 34,6% in severe asthma vs 12,5% in patients with moderate asthma (χ^2=5,3; gl=1; p<0,05). The study showed that the homozygous genotype *TNF-α* GG at position -308 has a protective role, being significantly more frequently identified in children with solitary form of asthma compared with those with allergic triad (86,2% vs 60,0%, respectively; χ^2=3,88; gl=1; p<0,05). Functionally compromised genotypes *TNF-α* GA+AA at position -308 were found more frequently in children with asthma associated with other allergic symptoms (40,0% in allergic triad and 55,6% in asthma cases associated with atopic dermatitis vs 13,8% solitary asthma, p<0,05).

Conclusions: The results of our study suggested an association between the IL-4 polymorphism at position -590 and asthma severity, and the association of the functionally compromised genotypes of the TNF-α polymorphism at position -308 with different clinical phenotypes of asthma in Moldovan children.

Key words: asthma, child, IL-4, IL-4Rα, TNF-α, gene, polymorphism, phenotype.

THE INFLUENCE OF BRONCHOALVEOLAR AND CIRCULATING TUMOR NECROSIS FACTOR-ALPHA ON APOPTOSIS IN DIFFERENT MODELS OF LUNG INJURY

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Cytokines are involved in a variety of lung diseases, but their pathogenetic role in programmed cell death is still controversial. This study tests whether the activation of an 'extrinsic' pathway to cell death is mediated by bronchoalveolar and circulating tumor necrosis factor (TNF)-alpha.

Nonlinear male rats weighing 200-230 g were used in all the experiments. For modeling of acid aspiration-induced acute lung injury anesthetized rats underwent tracheostomy and insertion of a fine-bore cannula into the anterior segment of the left lung. This was followed by the instillation of either 1.0 mL/kg HCI, pH 1.2 (n = 12) or 1.0 mL/kg saline in control rats (n = 12). All animals were studied at 6-hour after acid aspiration. For modeling of hepatopulmonary syndrome anesthetized rats underwent common bile duct ligation (CBDL) (n = 12). Sham rats underwent mobilization of the common bile duct without ligation (n = 12). All the animals were studied at 31-day after CBDL or sham operation. Bronchoalveolar lavage (BAL) and blood serum were analyzed for TNF- levels in pg/ml using commercially available ELISA kits. The level of apoptosis was analyzed with the help of Annexin V-FITS and propidium iodide using Beckman Coulter flow cytometer.

By 6 h after acid aspiration TNF-alpha values were significantly higher than in control group (in the blood serum: 17,06±1,91 pg/ml vs 11,54±0,59 pg/ml, p<0,001, in the BAL: 16,39±0,80 vs 1,73±0,13, p<0,001). It was also a significant increase in the number of early apoptotic cells present (in the blood serum: 0,63±0,14 vs 0,45±0,03, p<0,001, in the BAL: 2,41±0,15 vs 0,61±0,05, p<0,001). At 31-day after CBDL TNF-alpha values were also significantly higher than in control group (in the blood serum: 46,36±2,33 pg/ml vs 10,35±1,90 pg/ml, p<0,001, in the BAL: 11,50±0,77 vs 2,06±0,44, p<0,001). It was also a significant increase in the number of early apoptotic cells present (in the blood serum: 2,02±0,35 % vs 0,60±0,09 %, p<0,01, in the BAL: 2,77±0,45 % vs 0,47±0,06 %, p<0,01).

In acid aspiration-induced acute lung injury and hepatopulmonary syndrome the high level of TNF-α is positively correlated with the increasing level of early apoptosis. In the future there will be investigated TNF-α receptors: TNF-RI and TNF-RII.

THE INFLUENCE OF STANDARD TREATMENT OF PATIENTS WITH ACUTE ADENOVIRAL INFECTION ON THE CONCENTRATION OF INTERFERON-ALPHA, IMMUNOGLOBULINS OF BASIC CLASSES, THE ABSOLUTE AND RELATIVE NUMBER OF IMMUNOCOMPETENT CELLS IN THE PERIPHERAL BLOOD

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The remedial measures carried out according to a standard procedure adopted at the Chernivtsi base military hospital on 10 male patients aged from 19 to 24 years with acute adenoviral infection (AAI) have demonstrated a positive effect on the clinical course of the disease which was characterized by an improvement of the general level of health of the patients owing to an abatement of the symptoms of intoxication and a disappearance of the signs of the disease.

A course of administered standard treatment of AAI results in an essential tendency, in some cases, towards a reduction of the concentration of interferon-alpha (IFN-α) by 34,0% and immunoglobulins of the basic classes: IgM – by 9,3%, IgG – by 9,1% and IgA – by 10,3%/

A standard treatment administered to patients with AAI during three days contributes to a certain decline in the peripheral blood of the concentration of IFN of type I and immunoglobulins of the basic classes that may influence negatively on the resistance of the patients' organism to another viral or bacterial infection. Therfore, administering replacement therapy with the inclusion of IFN of type is necessary.

Treating patients with AAI by means of a standard method results in an improvement (normalization) of the absolute and relative amount of immunocompetent cells and immunohematological indices and coefficients due to an increase of the absolute and relative number of lymphocytes, the indices of nonspecific antiinfectious resistance and immune antiinfectious defence; a tendency towards a decrease of the absolute number of leukocytes, stab neutrophils, segmentonuclear leukocytes, monocytes and the immunohematologic indices and coefficients.

Irrespective of a positive effect of the standard method of treatment of patients with AAI one fails to achieve desired positive results, requiring toupdate this mode of treatment. Proceeding from the results obtained, one can come to a conclusion that this method, despite its efficacy, does not influence the increase of the concentration of endogenous cytokines (interferons) which perform an important antiviral and immunoregulatory function of nonspecific antiinfectious and specific immune antiinfectious defence.

Adenoviruses exert an interferonogenic effect – they stimulate the synthesis of endogenous IFN-α, but in case of AAI the standard treatment is not conducive to an elevated concentration of IFN-α, lowering the efficacy of the basic method of treatment. From our point of view, it is advisable to use replacement therapy to improve the results of treatment. Thus, an elaboration of a multimodality treatment of patients with AAI along with the use of replacement therapy of native and recombinant IFN-α against a background of basic standard therapy may improve the process of treating AAI.