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ENGLISH VERSION: IMBALANCE OF MUCOSAL IMMUNITY AT MODERATE AND SEVERE BRONCHIAL ASTHMA[*]

Beloglazov V.A., Popenko Yu.O.

State Institution "Crimean State Medical University Named After S.I. Georgievsky"

It is known that mucosal immunity is the first line of defense against foreign antigens. The objective of our study was to determine the state of mucosal immunity in patients with moderate and severe persistent bronchial asthma during background therapy. We examined 109 patients (63/57.8% of females; 46/42.2% of males) receiving outpatient treatment. All patients were divided into two groups: Group 1 – patients with moderate bronchial asthma (68 subjects with average score of 3,0±0,14 according to ACQ, FEV1-67,01±2,10%; Group 2 – patients with severe bronchial asthma (41 subject with average score of 4,06±0,12 according to ACQ, FEV1- 34,45±1,50%). The levels of total sIgA and anti-ET-sIgA were significantly increased in the study groups as compared to the normal value (p<0.01); no differences in this parameter among the groups were detected. Revealed changes of the mucosal humoral immunity reflect expressed antigenic stimulation of the mucosal immune system at the background of functional incompetence of the epithelial barrier which implements the phenomenon of endotoxin aggression

Key words: immunity, mucosal anti-endotoxin, bronchial asthma, secretory Ig A.

Mucosal immunity is a part of immune system represented by a mucous membrane which is aimed at the contact with antigens from the environment [1]. This kind of immunity consists of lymphoid tissue which is associated with mucosa (MALT or mucosa-associated lymphoid tissue) and may be divided into several components: gut-associated lymphoid tissue (GALT), bronchus-associated lymphoid tissue (BALT), nasal-associated lymphoid tissue (NALT), lymphoid tissue of mammary and salivary glands [1, 2].

Antigenic material is delivered to the interfollicular T cell-dependent zone of GALT Here, Th-cells secrete the whole package of cytokines: effects of transforming growth factor-β (TGF-β), which switches B-cells to produce IgA, for example instead of IgG or IgE, are the most studied. IgA-committed (i.e. obliged to produce exactly IgA) lymphocytes move away from the follicle into the mesenteric lymph nodes where they transform into plasmablasts [5].<0}

It is known that sIgA provides local protection of integrity and functioning of the mucosa by preventing attachment of microorganisms to these tissues and their penetration into the epithelial lining. It is also believed that sIgA can bind pathogenic microorganisms directly into the epithelial cells and also can bind antigens in the lamina propria of mucosa, as well as move them through the epithelial layer to the mucosal surface, thus releasing the organism from locally formed immune complexes and reducing the likelihood of their entry into systemic circulation [3,4].

Materials and methods of the study

Objective of our study was to determine the state of mucosal immunity in patients with moderate and severe persistent bronchial asthma during background therapy.

In order to achieve the objective, assigned task was to study the state of local, general (secretory Ig A) and anti-endotoxin (secretory anti-ET IgA) immunity in this category of patients. We examined 109 patients (63/57.8% of females; 46/42.2% of males) receiving outpatient treatment of the underlying disease in accordance with the order of the Ministry of Health of Ukraine dated March 19, 2007 No. 128, who received salmeterol at a dose of 50-100 μg/day and fluticasone propionate at a dose of 500-1000 μg/day. The level of control over the patients with bronchial asthma was analyzed using Asthma Control Questionnaire (ACQ) designed by Elizabeth Juniper (1999). ACQ consists of 7 questions filled out by the patient: 5 of them relate to the severity of the most important symptoms (nocturnal/awakening symptoms, daytime asthma symptoms, limitation of daily activity, shortness of breath, wheezing), the use of emergency drugs and FEV1. Severity of symptoms was evaluated using a visual analogue scale with score ranging from 0 points (no symptom) to 6 points (maximally expressed symptom). The average score of 0.75 was considered the upper limit of controlled asthma; the average score ranging from 0.75 to 1.5 was considered as partially controlled and 1.5 or higher average score – as uncontrolled asthma.

All patients were divided into two groups: Group 1 – patients with moderate bronchial asthma (68 subjects (62,4%), with average score of 3,00±0,14 according to ACQ, FEV1-67,01±2,10%; Group 2 – patients with severe bronchial asthma (41 subject 37,6%), with average score of 4,06±0,12 according to ACQ, FEV1- 34,45±1,50%.

Secretory anti-endotoxin immunoglobulin A (anti-LPS-sIgA) and total immunoglobulin A in induced sputum were measured by enzyme-linked immunosorbent assay (ELISA) according to the protocols developed in the Clinical Immunology Lab of the Central Research Laboratory of Crimean State Medical University named after S.I. Georgievsky. All

obtained results were statistically processed using nonparametric criteria via the program «MedStat» (serial number MS0011) DNPP TOV "Alpha", Donetsk.

Results and their discussion

The state of mucosal immunity in BA patients was assessed by the level of anti-ET-sIgA and total IgA in the induced sputum of this category of patients.

The level of total secretory IgA and anti-ET-sIgA in BA patients is presented in the table.

Table

The level of total secretory IgA and anti-ET-sIgA in the induced sputum of BA patients<0}

Group	Number of studies	Mean value, Me(quartile I-III) mg/L Statistic parameter (p)	Mean value, Me (quartile I-III) optical density unit Statistic parameter (p)
Normal value	23	31.10 (15.00-41.8)	0.037 (0.030-0.053)
Group 1<0}	68	66.75 (36.4-106.5) <0.01	0.193 (0.141-0.297) P<0.01
Group 2	41	66.60 (37.75-109.55) P<0.01 P1 >0.05	0.195 (0.152-0.274) P<0.01 P1 >0.05

Note: P – significance of differences from the normal value
P1 - significance of differences between Groups 1 and 2 <0}

The table above demonstrates that the level of total sIgA was significantly increased in the study groups as compared to the normal value (p<0.01); no differences in this parameter among the groups were detected. On the other hand, the level of anti-ET-sIgA in Groups 1 and 2 of BA patients was elevated (p<0.01) as compared to the normal value. No differences in this parameter were revealed during the study between Groups 1 and 2.<0}

Thus, parameters characterizing mucosal humoral general and anti-endotoxin immunity were increased in moderate and severe bronchial asthma; meanwhile, the decrease of anti-ET-sIgA was detected according to the literature data in mild BA with sIgA not exceeding the normal range [6]. High level of sIgA is considered as a reflection of intense antigenic stimulus of mucosa and a high level of humoral antibody response. Thus, elevated level of total sIgA was detected in patients with non-specific ulcerative colitis (NUC), and elevated level of anti-ET-sIgA was observed in patients with Crohn's disease (CD) [7]. Is compensatory consolidation of mucosal barrier physiologically adequate? Judging by the fact that both in NUC and CD elevated translocation of ET into the internal environment of the body are registered, this consolidation of mucosal barrier functionally cannot prevent endotoxin aggression. Incompetence of mucosal anti-endotoxin immunity may be associated both with the molecule of anti-ET-sIgA itself (low affinity to ET) and with violation of the mucosal barrier at the level of interepithelial junctions, resulting in dramatically increased intestinal permeability to various xenobiotics, including ET. Moreover, anti-endotoxin aggression in severe asthma may be associated with increased shunt blood flow (bypassing the liver through the portocaval anastomoses) due to activation of the sympathetic nervous system and the use of significant doses of β2-sympathomimetic drugs [8]. Anyway, both in severe BA, in NUC and CD, activation of mucosal humoral immunity on mucous membranes requires prescription of a powerful anti-inflammatory and suppressive (from a perspective of influence on the immune response) therapy modulating effects of proinflammatory mediators and factors, among which ET plays a potentially important role.

1. In groups of patients with severe and moderate persistent BA the level of secretory anti-ET-IgA in the induced sputum is 5.3 times (p<0.01) higher than the value of this parameter in the group of healthy donors. No intergroup differences of this parameter were revealed.<0}

2. In BA patients from clinical groups 1 and 2 the level of secretory IgA is 2.2 times (p<0.01) higher than the value of this parameter in the group of healthy donors.

3. Revealed changes of the mucosal humoral immunity reflect expressed antigenic stimulation of the mucosal immune system at the background of functional incompetence of the epithelial barrier which implements the phenomenon of endotoxin aggression.

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