THE ASSOCIATION OF FUNCTIONAL (SPIROGRAPHIC AND PEAK FLOW METRIC) CHARACTERISTICS AND CLINICAL EVALUATIONS OF BRONCHIAL ASTHMA CONTROL IN CHILDREN AND TEENAGERS

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The aim of the investigation is to estimate the association of bronchial asthma control level indices according to Asthma Control Questionnaire (ACQ) with indices of peak expiratory flow (PEF) and forced expiratory volume 1-second (FEV1) measured simultaneously with the interviewing.

Materials and Methods. There were examined 127 children and teenagers aged 5–17 years with atopic asthma of various levels of asthma control. Apart from standard clinical (including anthropometry), functional, immunologic, allergological examinations, all children underwent questionnaire survey according to ACQ, PEF measurement using peak-flowmetry, and the measurement of basic spirographic indices.

Results. There was revealed the correlation relationship between ACQ test indices (in points), for one part, and PEF and FEV1 (in percentage of adequate values) measured in the daytime, for the other part. The correlation coefficient between ACQ and FEV1 was -0.65, p=0.00001, that is higher than the coefficient between ACQ and PEF (r=-0.39; p=0.00001). To estimate the potential contribution of data of functional parameters in the diagnostics of asthma control there was performed discriminative analysis. A part of correctly classified cases relying on functional parameters was 53% for PEF and 66% for FEV1, i.e. the classification of bronchial asthma control level with the assistance of FEV1 monitoring has advantages as compared to PEF measurements.

Key words: bronchial asthma; bronchial asthma control methods; Asthma Control Questionnaire; spirographic characteristics; Peak Flow metric characteristics.

The prevalence of bronchial asthma (BA) reaches 5-10% in children population. Pathogenetic mechanisms of its development in children age are associated mainly with atopy and IgE-dependent chronic allergic inflammation in airways [1]. Inflammation in BA is of persisting character and determines the intensity of the disease clinical manifestations [2]. Modern conciliation documents state BA therapy to be aimed at asthma control carried out through anti-inflammatory therapy [1, 3]. The implementation of the concept into clinical practice along with pharmacology development has enabled to succeed in BA treatment. However, epidemiological surveys indicate that a proportion of patients with controlled asthma course in actual clinical practice do not approximate 50% yet [4], therefore, along with the improvement of approaches to disease pharmacotherapy, great attention is paid to the development of optimal BA control diagnostic methods including those for children and teenagers [5].

Currently, the following BA control diagnostic and monitoring methods are recognized as basic [1, 3]:

Clinical judgment of BA course according to the criteria specified in conciliation documents;

Questionnaire use (ACT, ACQ, NAEPP, etc);

Study of functional parameters (measurement and monitoring findings of peak flowmetry, spirography, including provocation tests);

Determination of inflammation biomarkers in systemic and organ-specific substrates.

Specialists assess the information capacity of these techniques in BA control in different ways; some researchers find no significant correlation relationship between separate methods of asthma diagnostic control that gives the evidence of existing contradictions and uncertainty of the problem in general [6–8]. The existing various readings of the findings of clinical and functional control methods

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cause further pursuance of the researches on comparing information capacity of different techniques.

The aim of the investigation was to estimate the association of bronchial asthma control level values according to Asthma Control Questionnaire (ACQ) with values of peak expiratory flow and forced expiratory volume 1-second measured simultaneously with the interviewing.

Materials and Methods. The study was carried out on the basis of Nizhny Novgorod Children Clinical City Hospital No.1. We examined 127 children aged 5-17 years mainly with atopic BA of various levels of asthma control. Apart from standard clinical (including anthropometry), functional, immunologic, allergological examinations, all children underwent questionnaire survey according to ACQ, peak expiratory flow (PEF) measurement using peak-flowmetry, and determination of main spirographic indices - forced expiratory volume 1-second (FEV1), forced vital capacity (FVC), Tiffeneau index; in some children - in the course of the disease. Altogether, we carried out 242 investigations on simultaneous assessment of ACQ test, peak flowmetry findings and basic spirographic parameters. The researches were performed during daylight hours (!), 4-5 h after taking systemic and inhalation medications. We did not change inhalation rate and amount administered by an attending doctor

For clinical judgment of BA control level we used a cut version of Asthma Control Questionnaire (ACQ, Russian version) developed by E. Juniper et al. [9]. The advantage of the test is the possibility of dynamic monitoring of disease symptoms, since they are estimated at one-week interval. There is also an extra version of the questionnaire — "ACQ-diary" that enables to monitor asthma symptoms daily. In accordance with the recommendations of the test, BA was referred to as controlled if the score was lower than 0.75 (group 1); partially controlled (group 2) — from 0.75 to 1.5; if test value was over 1.5, no disease control was stated (group 3) [10].

PEF was determined by peak flowmetry using Peak Flow Meters of one manufacturer (Vitalograph, Ireland), calibration — according to EN ISO 23747: 2007. It excluded the falsification of the findings due to potential inconsistency of calibrations when Peak Flow Meters of different manufacturers are used. Then we calculated percentage ratio of the measured PEF values in relation to adequate values of this parameter (www. Peakflow.com).

The basic spirographic indices — FEV1, FVC, Tiffeneau index — were determined using portable spirometer — Ventilograph (Vitalograph, Ireland).

Functional parameters were measured at examination with frequency of 3–5 times, and then averaged PEF and FEV1 were used.

According to the recommendations, the results were statistically processed using Statgraphics plus [11, 12]. The data are presented as $M\pm m$, where M — mean, m — mean square deviation. The differences of parameters between the groups were assessed by means of dispersion analysis ANOVA by Duncan ranking test (Multiple Range Test). The differences were statistically significant if p<0.05.

Results and Discussion. ACQ mean values in group 1 (86 patients, 142 investigations) were 0.20±0.24 points

(controlled course of the disease), in group 2 with partially controlled asthma (45 patients, 50 investigations) — 1.07 ± 0.24 points; and in group 3 with uncontrolled BA (38 patients, 49 investigations) — 2.48 ± 0.72 points.

"ACQ — forced expiratory volume 1-second" correlation relationship. The obtained data (Table 1) indicate the presence of highly reliable correlation relationship between ACQ score and FEV1 (R=-0.65 when p=0.00001).

Taking into account the revealed correlation dependence between "single-step" control assessment using ACQ and FEV1 value we calculated 95% of confidence intervals (95% CI) of FEV1 values for groups with different BA control level estimated by ACQ test (Table 2). The obtained data indicate that as the control level in BA patients is decreasing, there is observed the expected reduction of mean FEV1 values. We revealed statistically significant differences of this parameter values in patients with controlled, partially-controlled, and uncontrolled asthma (Table 3).

FEV1 values in children with controlled BA, ACQ values of which are lower 0.75, averaged 94.3±11.8%. They were statistically significantly higher than those in patients with partially controlled and uncontrolled course of the disease. FEV1 level in patients with partially controlled asthma was higher than in patients with uncontrolled course of the disease, but lower compared to those in children with controlled asthma, and averaged 81.3±8.9%.

The lowest FEV1 values were found in patients with no

Table 1

Equations of correlation between ACQ score and parameters FEV1 and PEF (221 examinations)

Parameters	Equation	R	р
For FEV1	ACQ=4.33-0.04.FEV1	-0.65	0.00001
For PEF	ACQ=2.70-2.07.PEF	-0.39	0.00001

Table 2

FEV1 indices (% of adequate values) in children with different asthma control estimated by ACQ

Indices	Groups (according to ACQ)		
marooo	1 st	2 nd	3 rd
Mean	94.3	81.3	72.4
Standard deviation	11.8	8.9	14.2
Minimum-maximum	76.5–132.0	63.3–101.0	42.5-95.5
95% CI	92.5–96.2	77.9-84.6	69.0-75.4
Statistics	F=	36.72; p=0.000)1

Table 3

Statistical significance of differences of FEV1 values in groups with different asthma control estimated by ACQ

Groups	Intergroup difference coefficient and the limit (in brackets) according to Multiple Range Test	
1–2	13.07 (5.39)*	
1–3	21.93 (5.39)*	
2–3	8.86 (6.63)*	

* — differences are statistically significant.

asthma control — 72.4 \pm 14.2%. However, in this group there were patients with FEV1 exceeding 90% of the adequate norm. As a rule, these patients received adequate therapy for BA exacerbation with marked positive effect, and by the end of the examination day they felt much better. In the end, they had more favourable judgment according to "ACQ–diary" than according to "ACQ–week" scale, and were accompanied by the improvement of functional parameters.

"ACQ — peak expiratory flow" correlation relationship. The study of correlation relationship between the control level evaluation using ACQ test and peak flowmetry values calculated as related to the parameters of population norm (Table 4), revealed R=-0.39 when p=0.00001, and it is significantly lower than the relationship between ACQ and FEV1 values.

The results of calculations of mean values and 95% CI of PEF values (as related to adequate values) in asthma patients with different control level estimated according to ACQ scale (Table 5) indicate that in the context of modern therapy, day PEF levels in patients with controlled BA generally are close to those of population norm. As the control characteristics deteriorate, there is observed regular decrease of these values. However, it is noteworthy, that in modern clinical practice PEF values in patients with controlled and partially controlled asthma in the daytime remain sufficiently high relating to mean population norms and amount to 96.3±11.8 and 81.3±8.9% respectively. In patients with no disease control PEF diagnosed according to ACQ scale as related to the norm, on the average are lower than 80%, and amount to 72.4±14.2%; 95% CI in this group is 74.0-84.0%.

Taking into account that FEV1 and PEF were found to have correlation relationship with ACQ test values,

Table 4

PEF (in % of adequate PEF values) in children with different asthma control according to ACQ assessment

Groups	Groups (according to ACQ)		
(according to ACQ)	1 st	2 nd	3rd
Mean	96.3	84.9	78.9
Standard deviation	17.9	15.2	17.7
Minimum-maximum	65.0–132.7	56.4-122.2	35.5–116.5
95% CI	93.8–99.0	80.0–90.0	74.0-84.0
Statistics	F=12.69; p=0.00001		

Table 5

Statistical significance of differences of PEF values (% of adequate values) in groups with different asthma control estimated by ACQ

Groups	Intergroup difference coefficient and the limit (in brackets) according to Multiple Range Test	
1–2	11.5 (7.4)*	
1–3	17.5 (0.08)*	
2–3	6.0 (9.1)	

* — differences are statistically significant.

Table 6

The results of discriminative analysis — classification of asthma control level according to findings of ACQ-test and the results of functional studies

Parameter	The number of properly classified cases, %	р
PEF	53.43	0.00001
FEV1	65.84	0.00001

and therefore, with BA control level estimated by ACQ scale, we performed discriminative analysis to assess potential contribution of these functional parameters into the diagnosis of disease control (Table 6). The number of properly classified cases based on functional parameters was 53% for PEF, and 66% for FEV1. Thus, in general, the classification of BA control level with the assistance of FEV1 monitoring has its advantages in comparison with determination of PEF.

Conclusion. The study of bronchial asthma control level in children and teenagers revealed the correlation relationship between ACQ test score, for one part, and PEF and FEV1 (in percentage of adequate values) measured in the daytime, for the other part. The correlation coefficient between ACQ and FEV1 was -0.65, p=0.00001, that is higher than the coefficient between ACQ and PEF (r=-0.39; p=0.00001). The stated correlation levels between clinical judgment of symptoms and functional parameters conflict with neither clinical nor pathogenetic concept of the disease, since bronchial asthma symptoms are not due to the changes of patency of airways only, but have more complicated genesis.

The findings of discriminative analysis demonstrated that in general the classification of bronchial asthma control level in children with the assistance of FEV1 monitoring has advantages as compared to PEF measurements. Although the studied functional parameters measured in the daytime cannot be considered as exhaustive characteristics when determining bronchial asthma control level, they certainly can and should be taken into account in objective monitoring of asthma patients.

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References

1. Natsional'naya programma: Bronkhial'naya astma u detey. Strategiya lecheniya i profilaktika [National program: Bronchial asthma in children. Strategy of management and prevention]. Moscow: Russkiy vrach; 2008; 107 p.

2. Tillie-Leblond I., Montani D., Crestani B., de Blic J., et al. Relation between inflammation and symptoms in asthma. *Allergy* 2009; 64(3): 354–367.

3. GINA (Global strategy for asthma management and prevention). Updated 2011. http://www.ginasthma.org/uploads/users/files/GINA_ Report_2011.pdf.

4. Chapman K.R., Boulet L.P., Rea R.M., Franssen E. Suboptimal asthma control: prevalence, detection and consequences in general practice. *Eur Respir J* 2008; 31: 320–325.

5. Oppenheimer J.J., Li J. Attaining asthma control: measures of asthma control. *Curr Opin Allergy Clin Immunol* 2006; 6(2): 119–123.

6. Shingo S., Zhang J., Reiss T.F. Correlation of airway obstruction and patient-reported endpoints in clinical studies. *Eur Respir J* 2001; 17(2): 220–224.

7. Sharek P.J., Mayer M.L., Loewy L., Robinson T.N., Shames R.S., Umetsu D.T., Bergman D.A. Agreement among measures of asthma status: a prospective study of low-income children with moderate to severe asthma. *Pediatrics* 2002; 110(4): 797–804.

8. Khalili B., Boggs P.B., Shi R., Bahna S.L. Discrepancy between clinical asthma control assessment tools and fractional exhaled nitric oxide. *Ann Allergy Asthma Immunol* 2008; 101(2): 124–129.

9. Juniper E.F., Svensson K., Mork A.-C., Stahl E. Measurement properties and interpretation of three shortened versions of the asthma control questionnaire. *Respiratory Medicine* 2005; 99(5): 553–558.

10. Juniper E.F., Bousquet J., Abetz L., Bateman E.D. Identifying "well-controled" and "not well controled" asthma using the asthma control questionnaire. *Respiratory Medicine* 2006; 100: 616–621.

11. Glants S. *Mediko-biologicheskaya statistika* [Biomedical Statistics]. Moscow: Praktika; 1999; 459 p.

12. Dyuk V., Emanuel' V. *Informatsionnye tekhnologii v medikobiologicheskikh issledovaniyakh* [Information technology in biomedical researches]. Saint Petersburg: Piter; 2003; 528 p.