

MONDAY, SEPTEMBER 4TH 2006

261. Asthma – Miscellaneous issues

E2877

HFA vs CFC beclomethasone dipropionate – comparative effectiveness in asthma management

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The aim of our study was to compare the effectiveness of basic treatment of moderate – severe bronchial asthma patients with HFA BDP in half dose vs CFC BDP in full dose.

Materials and methods: 30 stable moderate-severe asthma patients (male 14, female 16, in the age 18 – 60 years, FEV₁ (56,8 ± 2,6) %) were randomised 1:1 to receive HFA BDP 250 mcg (I group) BID or CFC BDP 500 mcg (II group) BID during 3 months study period. Salbutamol PRN was allowed as rescue medication. Groups were comparable by age, sex, duration and severity of asthma.

Dynamics of asthma score, use of rescue medication (according diaries of self-observation), data of spirometry (FEV₁, FEF_{25-75%}) “MasterLab”, Erich Jaeger) were studied at the beginning of the investigation, after 1 and 3 months of therapy.

Results: the significant (p<0,01) decrease of asthma score from (4,6 ± 1,1) till (2,1 ± 0,8) in I group, from (4,7 ± 1,2) till (2,9 ± 1,3) in II group at the end of treatment course was observed. Mean use of rescue medication decreased from (4,3 ± 1,2) to (1,1 ± 0,4) puffs after 3 months in I group and from (3,9 ± 1,5) to (1,8 ± 1,1) in II group.

FEV₁ significantly improved in both groups, but FEF_{25-75%} - only in I group – from (45,7 2 ± 3,9) till (68,7 2 ± 4,1)%.

Conclusion: the dynamic of clinical-functional indices was more expressive in HFA BDP group, where BDP was in half dose because of the particularities of deposition of medicine due to different types of propellents. HFA BDP was effective in middle and small bronchi, that is of great importance in asthma. These results it is necessary to take into account while prescribing BDP with different types of propellent.

E2878

An approach of one-week treatment of inhaled corticosteroid for a diagnosis of asthmatic syndrome

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Asthma-like symptoms are shown in not only asthma but also pseudo-asthma including mitral valve disorder, allergic rhinitis and Sjögren syndrome with airway hyperresponsiveness. In this study, we assessed an approach of one-week treatment of inhaled corticosteroids (ICs) for a diagnosis of asthmatic syndrome. One hundred and twenty six subjects who had episodes of wheezing at night and/or early morning were included in this study. Asthma is diagnosed by a classical definition for asthma determination proposed by Ciba symposium and a clinical observation for two years after treatment with ICs. Clinical response of ICs was assessed on the basis of symptom score as visual-analogue scale and clinic peak expiratory flow rate (PEFR). Ninety-four of 126 subjects (75%) were diagnosed as asthma, where the 32 remaining participant were accepted as pseudo-asthma due to a diagnosis of another cause. Asthmatic but not pseudo-asthmatic patients showed that symptom score and clinic PEFr were improved by treating with ICs within one week. In this study, we demonstrated that an approach of one-week treatment of ICs was an effective tool for a diagnosis of asthmatic syndrome.

E2879

A randomized, double-blind, placebo-controlled study to evaluate the role of formoterol in management of acute asthma

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Background: formoterol, with fast- and long-acting profile, is effective in all types of asthma, however, few studies have addressed the use of it in asthma attack. This

MONDAY, SEPTEMBER 4TH 2006

study evaluated the efficacy and tolerability of low dose formoterol delivered by Aerolizer with that of salbutamol delivered by MDI.

Methods: 60 adult patients with acute exacerbation of asthma were randomly assigned to: group 1, a total dose of 600 µg salbutamol (200+200+200), delivered by MDI into spacer at 20-minute intervals; group 2, formoterol 24 µg (12+12) as two dry powder capsules via Aerolizer, at 20-minute intervals. As placebo, the patients in the salbutamol group also received two capsules, containing lactose and patients in the formoterol group received an identical MDI placebo concurrently. Peak Expiratory Flow Rate (PEFR) was measured at base-line, and 5 minutes after 2nd and 3rd doses.

Results: 60 subjects received salbutamol (n = 28), or formoterol (n = 32). Age, gender, baseline PEFR and previous medication were balanced in groups. Mean PEFR increased significantly over base-line in both groups (63% in salbutamol, p = 0.001 and 55% in formoterol, p = 0.001). Groups were not different in terms of the increase in PEFR (p=0.99). The adverse events were similar.

Conclusion: formoterol was found to be as safe and effective as salbutamol in management of acute asthma; We found that the Aerolizer could be adequately used in acute asthma and the control of the asthma attack doesn't need a high dose of formoterol as it's been used in previous studies. Further studies are needed to compare the long term effect of formoterol with salbutamol in acute asthma. MDI = meter-dose inhaler.

E2880

Effects of adding salmeterol to inhaled corticosteroids on lung function and quality of life in patients with mild persistent asthma

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It is advised that patients with mild persistent asthma are to be treated only with inhaled corticosteroids (ICS). We investigated the effects of adding salmeterol (S) to ICS in treatment of these pts on their quality of life.

In randomized cross-over study we treated 48 pts with combination of ICS and placebo (P) and ICS and S for 4 weeks each, and measured PEF and FEV₁ and determined mini Asthma Quality of Life Questionnaire (mini-AQLQ) total score before and after each period of treatment. Minimal important difference (MID) of total mini AQLQ score was defined as 0.5.

Mean values of PEF and FEV₁ were significantly better after treatment with ICS + S than after ICS + P (500.64 vs. 492.55, p < 0.05; 3.63 vs. 3.49, p < 0.01; respectively). After treatment with ICS + P 75% of pts experienced improvement, 20.8% deterioration and 4.2% remained the same. After treatment with ICS + S 79.2% experienced improvement, 14.6% deterioration, and 6.3% remained the same. We found no significant difference between distributions of effects of placebo and salmeterol on total mini AQLQ score. Number needed to treat was 23.81.

We concluded that, while adding salmeterol to ICS in pts with mild persistent asthma significantly improves their lung function parameters, its influence on their quality of life does not differ over placebo, probably because of significant placebo effect noticed in our pts.

E2881

Efficacy of the using budesonide/formoterol in patients with bronchial asthma (BA): the study of routine clinical practice

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The most of modern antiasthmatic drugs (incl. budesonide/formoterol, "Simbicator") demonstrate high effectiveness in clinical trials. On the other side, clinical efficacy usually less than in clinical trials.

Aim: Assess real effectiveness of budesonide/formoterol in routine clinical practice.

Methods: 120 general practitioners GP from different towns of Russia participated in this study in 2005. We received asthma control questionnaires (ACQ) from their outpatients, who used budesonide/formoterol during 3-4 months. Budesonide/formoterol was prescribed in dose 80/4,5µg twice a day for 14% patients and 160/4,5µg three times a day for 86% patients.

Results: We analyzed 1045 ACQ (mean age of patients was 50,3 (37,76-62,80) y.o., mean asthma duration- 11,4 (10,83-11,88) y. 38,5% patients had persistent intermittent, 21,2%-moderate, 40,3%-severe BA. Before starting budesonide/formoterol 17% patients did not use iGCS at all, 47% used iGCS, 16%- iGCS+LABA, 19%-oral GCS. Using budesonide/formoterol provided decreasing daily doses iGCS: before starting the patients received 830,6 (782,9-878,3)µg iGCS, after-566,7 µg (548,5-584,8) p=0.0001. After 3 months of treatment a part patients with total control increased from 2 to 36%. The mean days without night symptoms increased from 13,5±11,26 to 27,5±6,29 per months (p<0.0001); without day symptoms from 5,4±9,3 to 21,3±11,71 (p<0.0001); without relief medications from 5,7±11,75 to 19,9±11,90(p<0.0001).

Conclusion: Efficacy of the using budesonide/formoterol in routine clinical practice is comparable with clinical trials results.

E2882

Cost-effectiveness of budesonid/formoterol inhaler in treatment of moderate bronchial asthma

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We present results from open, randomized, comparative trial that was carried out in 16 cities of Russia. During 6 months 300 outpatients were observed, 150 from them were prescribed budesonid/formoterol, 150 continued anti-inflammatory therapy prescribed earlier (typical practice of treating patients). 103 patients from them received inhaled corticosteroids 800-1600 mcg as monotherapy, 21 patient received inhaled corticosteroids in a combination with long-acting β₂-agonists and 26 patient received cromons. The degree of restriction of physical activity, frequency of day time and night attacks were estimated on a scale in 5 points (0-absence of the infringements, 2-4- moderate and heavy infringements) Application of budesonid/formoterol has shown the best results by all criteria of clinical efficiency. The increase of FEV₁ by the end of research (20% on a median) was significantly greater in group of budesonid/formoterol than in control group (11%). Cost of treatment (cost of drugs and physician visits) was somewhat higher in budesonid/formoterol group. Average cost-effectiveness ratio showed that the cost per % increase of FEV₁ in group of budesonid/formoterol (484,08 rubles for the 1 month, 1742,68 rubles for 6 months) was lower than in group of comparison (1131,56 rubles and 2468,86 rubles). Cost per patient with absence of moderate or heavy infringements on all used scales at the end of study also was lower in the first group (9220,54 rubles for the 1 month; 44684,15 rubles for 6 months) than in the second group (11911,13 rubles, 59037,78 rubles). In conclusion budesonid/formoterol is cost-effective in treatment of bronchial asthma.

E2883

Efficacy of salmeterol/fluticasone pMDI versus DPI in patients with asthma

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We compared the bronchodilating effect of salmeterol/ fluticasone (S/F) from a multi dose dry powder inhaler (DPI- Seretide® Multidisk) to a pressurized metered dose propellant-free inhaler (pMDI) in 104 patients with asthma. Adults (mean age 51.7 years; FEV₁ ≤80% of predicted; 63 male) were randomized into parallel-group, pilot study to receive: 1. S/F-50/250µg via pMDI (n=32); 2. S/F-50/250µg via DPI (n=36); 3. S/F-25/125µg via pMDI (n=36). Lung function test was performed in 1, 3, 10 and 30 minutes after inhalation of the study drug.

There was the same onset of actions of both formulations in 1 minute after inhalation. The increase in FEV₁ 3 min was greater for S/F-50/250µg doses (17,9% and 18,04% respectively versus 14,87% for 25/125µg dose p< 0,001). The same pattern was seen for FEV₁ and MEF₂₅₋₇₅ parameters in 10 and 30 minutes.

We did not find evidence of a difference between the efficacy of S/F DPI and pMDI in patients with asthma. S/F pMDI is the equivalent to a DPI at the same dose.

E2884

Evaluation of adherence of patients with asthma to treatment by single combination inhaler

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"Cooperation" (CP) more than "compliance" reflects patients' willing and ability to follow doctor's recommendations.

Aim: In accordance with CP criteria adherence of patients with asthma to treatment by adjustable maintenance dosing (AMD) single combination inhaler Budesonid/formoterol (B/F) - Symbicort® turbuhaler® 160/4.5µg in comparison with two multiple fixed dosing inhalers (ICS and bronchodilators) was studied.

Methods: CP was evaluated by questionnaire IcBA-50 (original Russian Questionnaire). The study included 31 patients with asthma (mean age - 54.5±11.9 years), group A, treated by two multiple fixed dosing inhalers for years. All patients were supervised in clinic as outpatients and their CP was evaluated initially and in 6 months.

Results: There were no changes in degrees of CP of patients in group A, treated by two inhalers. Afterwards 26 of (group B, mean age - 52.5±13.3 years) started to take B/F initially 1-2 inhalations twice daily, depending on severity of asthma. Patients changed the dose to maintain asthma control by themselves. Patients were supervised in clinic as outpatients during another 6 months. CP was evaluated before starting B/F and in 6 months of treatment. CP parameters significantly improved after switching on B/F: "initial CP level" from 56.9±9.7% to 63.2±7.7% (p<0.01), "level of knowledge" from 38.2±9.9% to 45.6±9.6% (p<0.001), "level of the patients' satisfaction with the CP" from 89.9±5.4% to 94±5.1% (p<0.01), "total index of CP" from 62.5±5.6% to 65.9±5.4% (p<0.01) increased and decrease "comprehension of danger" from 39.8±14.8% to 34.9 ± 13.7% (p<0.01).

Conclusions: Patients treated by AMD B/F showed significant adherence to asthma treatment.

E2885**Efficacy of budesonide inhalation suspension in acute exacerbation of bronchial asthma in adults**

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Aim: To study the efficacy of budesonide inhalation suspension (BIS) (Pulmicort Respules, AstraZeneca) for treatment of acute exacerbation of bronchial asthma (BA) in adults.

Methods: 23 patients (7 men, 16 women) aged 19-75 years (mean age 53.8±11.0 years) with moderate or severe exacerbation of BA were included. All patients received bronchodilators and BIS 1-2 g per day via nebuliser "Pary Boy" for 4-10 days (on average 5.9±1.7 days).

Results: Towards the end of the treatment, all patients showed clinical improvement as reduction of asthma attacks from 5.5±2.6 to 1.8±1.8 per day ($p<0.001$) and the need in β_2 -agonists from 4.96±2.7 to 1.8±1.7 inhalations per day ($p<0.001$). Improvement of spirometry data was observed. PEF increased from 63.4±21.5 to 74.2±20.3% of pred. ($p<0.001$) and FEV1 increased from 54.6±19.6 to 67.1±16.2% of pred. ($p<0.01$), PEF variability decreased from 34.9±14.9 to 22.45±12.2% ($p<0.001$). The full control of BA (PEF≥80% of pred., lack of asthma attacks, normal physical activity) was reached in 13 patients (56.5%), partial control was obtained in 10 patients (43.5%). In induced sputum the total amount of cells decreased from 1.73±0.35 to 1.25±0.26·10⁶ ml⁻¹ ($p<0.001$), sputum eosinophils decreased from 23.6±16.5 to 10.3±4.9% ($p<0.001$), neutrophils decreased from 27.1±7.7 to 22.4±4.7% ($p<0.001$), macrophages increased from 47.4±12.8 to 64.6±5.9% ($p<0.001$).

Conclusion: The clinical study showed that BIS is effective in acute exacerbation of BA, but more studies are required to determine individual selection of dose and term of treatment.

E2886**The effect of inhaled fluticasone propionate on intraocular pressure of patients with bronchial asthma**

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The aim of this study was to investigate the influence of inhaled Fluticasone propionate on intraocular pressure (IOP) in asthmatics with primary open angle glaucoma with and without family history of glaucoma. 106 glaucomatous patients with visual field defects (Goldman perimeter), optic disc changes and elevated IOP (Goldmann applanation tonometry) and 39 control patients participated in the study. 22 asthmatic patients tested took 800 µg of Fluticasone propionate daily, and formed three groups: the first - 5 asthmatics with glaucoma and family history of glaucoma; the second 9 asthmatics with glaucoma without family history of glaucoma and the third 8 asthmatics without glaucoma.

The asthmatic patients with glaucoma and family history had higher IOP than those with glaucoma without family history 25.1±1.8 mmHg vs. 22.0±2.1 mmHg. ($p<0.05$; 28 eyes) and showed more severe visual field defects. Mean deviation 7.3 ±5.1 vs. 2.4±2.3 ($p<0.05$; 28 eyes), IOP was manual (15.6±2.2 mmHg) in all asthmatics without glaucoma except one patient who showed an ocular hypertensive response to Fluticasone propionate. The results support the hypothesis that the patients with family glaucoma inherit not only glaucoma disease but also increased sensitivity to Fluticasone propionate.

Conclusion: asthmatics on Fluticasone propionate that have family glaucoma need special care and treatment by ophthalmologist.

E2887**Pharmaco-economic analysis of the expenses connected with treatment of asthma**

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In the scientific work there was done the analysis of ambulance calls, which were connected with severe asthma exacerbations. Observation was during the year 2005 in Ukrainian city Vinnitsya, with population 358'403. 122540 calls were done to ambulance. 3190 of them were caused by asthma exacerbations, it makes 2.6%. 526 patients made those calls, from 1 to 2 calls were done by 382 patients (72%), 3-5 calls by 66 patients (12%), 6-10 calls by 31 patients (5.8%), 11-20 calls by 9 patients (1.7%), more than 20 calls - 38 patients (7.2%). So it is evident that the major part of the calls were done by the same patients. The expenses connected with providing of the first aid in the year 2005 were 255 200 UAH (49550\$). As the researches of the contingent of the patients, who make calls to the ambulance showed that they are of elderly and senile age, they have low level of education and do not follow the doctor's recommendations. For cutting of the costs, connected with providing of first aid to these patients, it is necessary to make them to follow the doctors' advices more thoroughly. We choose 17 patients that need more than 50 times per year assistance of the ambulance and we organized the group of volunteers. The volunteers were to proof whether the patients observe their basic treatment during the period of 6 months. It turned out that such an approach resulted in reduce of frequency of their calls to ambulance. During the observation period the number of calls reduced in 2,3 times, it led to considerable economy of budget means.

E2888**Mild asthma. Is constant therapy by inhaled steroids necessary?**

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Objective: the aim of this investigation was to evaluate the level of asthma control among patients with mild asthma who didn't get medical healthcare for a long time.

Materials and methods: 110 patients with asthma were actively studied by chest physician. All of the patients had a 5-year history of mild persistent asthma. The asthma control level was evaluated by ACT[®] test, lung function tests and questionnaires were performed, and quality of life was evaluated by SF-36.

The results of the investigation showed, that only 11% patients stepped down from level 2 to level 1 (intermittent). 49 patients with asthma of the level 2 (50%) had 3 exacerbations in the last year. Only 31,6% patients had constant controlling therapy by inhaled steroids with average dose 350 µg/daily of beclometazona dipropionatis. The result of ACT[®] test in this case was 20,5 (well control level). The result of the ACT[®] test of the patients with asthma who had irregular therapy by inhaled steroids (68,4%) was 18, that is lower ($p>0,05$). Comparison analysis of the lung function tests data and quality of life level didn't show differences between these 2 groups, as with a group of patients with intermittent asthma.

Conclusions: the results ACT[®] test and the evaluation of patients' quality of life don't demonstrate the benefit of the constant therapy by inhaled steroids under as-needed therapy in case of mild persistent asthma.

E2889**Inhalation of fluticasone propionate spray compared with theophylline as primary treatment for chronic mild to moderate asthma**

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Inhaled corticosteroids and oral theophylline are effective treatment for moderate asthma. The aim of this study was to compare benefits and adverse reaction of theophylline and aerosol fluticasone spray.

Methods: We included 40 patients with mild to moderate asthma. 20 of them received fluticasone propionate aerosol spray 125 mg two times per day during one year. The second group of 20 patients received theophylline twice per day in doses for optimum control of disease. The main outcome measure was daily diary of symptoms and peak flow rates, supplemental bronchodilator use hospital visits and absence from work, pyrometer measurements, bronchial provocation histamine tests.

Results: Both treatment strategies reduced symptoms and reduced absence from work and emergency treatment for asthma. Both had nearly normal pulmonary function. Fluticasone was significantly more effective in reducing symptoms, supplemental bronchodilators and systemic corticosteroids doses. Theophyllin caused more headache, insomnia, gastrointestinal distress and more patients had discontinued treatment because of side effects. Fluticasone caused more hoarsens. The risk/benefit profiles of these agents suggest that inhaled corticosteroids may be preferred agent.

E2890**Psychological peculiarities of asthmatics with thyroid pathology**

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53 asthmatics with thyroid pathology (autoimmune thyroiditis -36, Grave's disease - 17; group 1) and 28 asthmatics without it (group 2) were included in trial. The aim of study was to investigate psychological peculiarities of asthmatics with thyroid pathology. Psychological traumatic experience preceded development of thyroid disease in 38% of patient. Most of asthmatics with thyroid pathology showed high level of social activity. The high intellectual level was typical for patients of group 1. Large number of patients with thyroid disease (70.2%, $p<0.05$) had an intellectual work, especially among the patients with Grave's disease; in most of them (82%) work was associated with high professional responsibility; 82% of these patients have higher education. Characteristic psychological traumatic factors for asthmatics with Grave's disease were high professional responsibility and loss of sense of protectability. Stresses such as loss of vital incentive, disability, discharge, disappearance or death of near relation played more important role among psychological traumatic experience preceding development of hypothyroidism in asthmatics with thyroiditis. The importance of emotional disorders in exacerbation of asthma was increased in patients with hyperthyroidism and patients who were treated by thyroid hormone. These patients complained of sense of short breath and lump in the throat, increased sensitivity to smell and dust, they presented petulance, suffocation in stress situation. Thus, characteristic personality features are typical for asthmatics with thyroid pathology and thyroid disorders can change asthma course by means of emotional state.

E2891**Does satisfaction with inhaled asthma treatment correspond with spirometric parameters?**

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The aim of the study was to assess if the satisfaction with inhaled asthma medication in ambulatory patients (pts) correspond with spirometric parameters.

In 113 asthmatic pts (42 male, mean age 44 ± 17 years; mean FEV₁ 74.4 ± 23.5% predicted) we administered "Satisfaction with Inhaled Asthma Treatment Questionnaire" (SATQ), which scores are calculated for the overall satisfaction, as well as for the individual domains (effectiveness of treatment, ease of use, medication burden, and side-effects and worries). We measured following spirometry parameters: FVC(L), FVC% predicted, FEV₁(L), FEV₁% predicted, FEV₁/FVC x 100 and PEF(L). The same procedure was repeated in 41 out of 113 pts at the follow-up visit, with a mean 12-week interval between the visits.

Pearson's coefficient of linear correlation confirmed a highly significant correlation between the overall satisfaction and the values of all spirometric tests evaluated. The highest degree of correlation with overall SATQ scores was found for the values of FEV₁% predicted and FEV₁(L) (r = 0.410, p < 0.001 and r = 0.356, p < 0.001, respectively). We also noticed a statistically significant correlations between the values of FEV₁% predicted changes and changes of overall SATQ scores and medication burden domain scores (r = 0.384, p = 0.013 and r = 0.463, p = 0.002, respectively).

Reduced pulmonary function in asthmatics determined by spirometry strongly reflects impairment of their inhaled treatment satisfaction as assessed by means of SATQ.

E2892**Eosinophilic pneumonia in subjects with bronchial asthma: casual or causal relationship?**

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Acute eosinophilic pneumonia has been reported, as a kind of hypersensitivity pneumonitis related to drugs or allergens, but its frequency in patients with chronic asthma, well controlled under regular therapy on inhaled corticosteroids (ICS), has not been frequently described. We report 7 patients with chronic asthma, followed in our asthma clinic since 2 yrs at least, who complained recent onset of cough, associated with chest X-ray demonstration of pulmonary infiltrates and a marked elevation in eosinophil count in blood, sputum and/or BAL. Chest X-ray abnormalities were confirmed by CT, as multiple, often bilateral, infiltrates, which could migrate in different pulmonary lobes over time. Asthma symptoms and pulmonary function were stable in comparison with previous evaluations. In the past none patients showed peripheral hyper eosinophilia. Pulmonary infections or parasites were excluded by sputum and/or BAL cultures. A course of oral corticosteroids was performed, with resolution of symptoms, pulmonary infiltrates and hyper eosinophilia. Eosinophilic pneumonia can occur in subjects with chronic bronchial asthma, despite a well control of asthma symptoms and regular treatment with ICS. If this fact is a casual association or there is a relationship between asthma and eosinophilic pneumonia remain to be established.

Subjects	Duration of Asthma	Blood eosinophils (%)	Sputum eosinophils (%)	BAL eosinophils (%)	FEV1 (pred%)	Chest Xray/CT
# 1	18	37	14	68	35	Bilateral infiltrations
# 2	43	13	32.6	37	85	LLL infiltrations
# 3	2	32	80.2	-	66	Bilateral infiltrations
# 4	4	14	-	36	75	Bilateral infiltrations
# 5	30	15	-	15	85	RUL infiltrations
# 6	17	20	8.3	28	50	Bilateral infiltrations
# 7	25	7	-	7	80	RRL infiltration

E2893**The relationships between pulmonary functions, perception on dyspnea and inhaler usage skill in asthmatic patients**

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The importance of inhaler usage skill has been known in asthma. But there is not enough data about relationship between the degree of the importance of this ability and pulmonary functions. The aim of this study was to investigate the relationships between inhaler usage skill and pulmonary functions in control of asthma.

The study included 50 (F/M:44/6) stable asthma patients who have been given regularly training for inhaler adaptation. Peak expiratory flow (PEF) measurement by both spirometer and PEF meter, Modified Medical Research Council Dyspnea Scale (MMRC), inhaler technique scoring and demographic questions were

performed in two years interval. Paired-t test, Spearman correlation analysis and Wilcoxon test were used for statistical analysis. The score of inhaler usage skill increased after two years, but the difference was not significant. Perception of dyspnea and asthma severity did also not change. As expected in patients who had severe dyspnea grade according to MMRC; FEV₁, FVC, FEV₁/FVC and FEF₂₅₋₇₅ were significantly low (p=0.03). There was no meaningful relationship between spirometric values and score of inhaler usage skill (p>0.05). There was a significant relationship between the score of inhaler usage skill and increase of PEF measurements by PEFmeter (p=0.02). In conclusion training of inhaler adaptation affects only value of PEF measurement by PEFmeter. This could be explained with the ability of the patient to make the PEF manoeuvre. We did not determine any further relationship between inhaler adaptation and other objective control parameters of asthma.

E2894**Asthma in elite Brazilian swimmers: are we failing to diagnose? Evaluation by questionnaire and spirometry**

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Despite all of the advances in the management of asthma, current levels of disease control are far below the goals for long-term asthma management. Mild and exercise induced asthma (EIA) are very common reasons for poor development in sports. Based on the current belief that swimming can "cure" asthma, many children are encouraged to swim. The Olympic Committee established rules how to manage asthma in elite athletes, balancing optimal control and anti-doping regulations. There is no data relative to incidence of the disease in swimmers in Brazil. 38 elite athletes of Brazilian swimming team (17-30 y) were evaluated by ISAAC questionnaires (Q) and by spirometry (S). Q was divided into three groups: negative ("N") and positive ("P") for asthma and with some clinical clues (±). The cut off to normal (N) spirometry or obstructive (O) was FEV₁/FVC < 0.80. 29% started swimming due to respiratory problems.

Results: 13 athletes had normal Q and S (34,2% N/N); 5 had N Q and OS (13,2% N/O); 4 (10,5% P/N) reported asthma, with N S; 3 (7,9% P/O) had uncontrolled asthma; 5 had clinically suspected asthma or EIA (13,2% ±/N) and 8 had no previous diagnosis of asthma (21% ±/O).

Conclusion: Q and S are simple and effective methods of screening asthma. Asthma is very frequent in elite athletes. The awareness is very low, which may lead to a negative impact in their quality of life and performance. Asthmatic athletes should receive optimal treatment to compete in equal conditions. We urgently recommend that sports managers, coaches and athletes be educated about asthma diagnosis and control in order to positively impact the performance and overall quality of life of their athletes.

E2895**Quality of life and sinonasal symptoms in outpatient asthmatics**

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Sinonasal symptoms are frequently reported in patients with asthma. In randomly selected 65 asthmatic outpatients (41 female; mean age was 45 ± 17 years; mean FEV₁ was 75.9 ± 23.6% predicted; average disease duration was 13 ± 10 years), we evaluated the relationship between the severity of their sinonasal symptoms and quality of life (QoL).

Sinonasal symptoms were assessed by standardized questionnaire - Sino-Nasal Outcome Test (SNOT-20). Its scores range from 0 to 5, with a higher score indicating a greater rhinosinusitis-related health burden. The QoL was evaluated by three QoL questionnaires: two disease specific - the Mini Asthma Quality of Life Questionnaire (MiniAQLQ) and the St George's Respiratory Questionnaire (SGRQ), and one generic form - 15D. Total MiniAQLQ, SGRQ and 15D scores, as well as the scores for individual domains of MiniAQLQ (limitation of activity, asthma symptoms, emotional state, environmental stimuli) and SGRQ (symptoms, activity and impacts scores), were calculated for each patient.

Pearson's coefficient of linear correlation showed a highly significant correlation (p < 0.001) between all of the QoL scores and the values of SNOT-20 scores. The highest degree of correlation with sinonasal scores was found for the total MiniAQLQ and SGRQ scores (r = - 0.639 and r = 0.618, respectively).

Presence of sinonasal symptoms in asthmatics is strongly correlated with the impairment of the disease control. By achieving good asthma control, we expect that patients at the same time improve their sinonasal symptoms.

E2896**Assessment of symptoms, clinical findings and bronchial responsiveness in intermittent asthmatics**

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Preface: Patient with asthma frequently have poor recognition of their symptoms

perception of the severity, especially if their disease is severe and longstanding (1). Some relationship has been established between laboratory indices of airway hyperresponsiveness and PEF variability

We assessed the relationship between symptoms, clinical finding and airway hyperresponsiveness.

Methods: In 60 young asthmatics, nonsmokers, with symptoms over several years, but not in last two months, and with normal spirometry, histamine bronchoprovocation test was done.

Results: According to histamine responsiveness, patients were divided in two groups: First group with positive test (30 patients PC20=2.99±0.51 mg/ml), and second, 30 patients with negative test. FEV1 was in average 93.2% in the first, differing significantly from 101.8% in second group ($p<0.05$, Wilcoxon test). Symptoms were approximately equally distributed. Clinical finding was positive in 73% in the first and 28% in second group ($p<0.05$, Chi squared). Degree of hyperresponsiveness was in positive correlation with clinical findings ($p<0.05$, Spearman's rho) but not with FEV1.

Conclusion: Positive clinical finding, but not FEV1 values, can indicate the extent of bronchial responsiveness to histamine in intermittent asthmatics. Findings on symptoms as an individual expression could not indicate the severity of asthma.

1. Killian KJ, Summers E, Watson RM, O Byrne PM. Factors contributing to dyspnea during bronchoconstriction and exercise in asthmatic subject. *Eur Respir J* 1993;6:1004-10.

E2897

A randomized double-blind placebo-controlled trial on the short and long-term effects of electro acupuncture on moderate to severe asthma

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Objective: The objective of this study was to assess short and long-term effects of electro acupuncture in asthma.

Methods: A randomized, double-blind, placebo-controlled trial was performed in 34 subjects with moderate to severe persistent asthma. After initial visit, eligible subjects were randomized to receive one of the following therapies:

Low frequency electro acupuncture (5 Hz, stimulation intensity equals patient's tolerance threshold) for ten sessions in addition to their usual asthma medications ($n = 16$), sham electro acupuncture and their usual medications ($n = 10$), or usual medications alone ($n = 8$). Each group was followed weekly for a month after the last session of electro acupuncture and also after the next two consecutive years. The primary outcome was change from baseline in forced expiratory volume in 1 second (FEV1). Secondary outcomes were FEV1, FVC, MEF50, daily rescue medication use, percentage of nighttime awakenings due to asthma, emergency department visits/hospitalizations, improvement sensation rate.

Results: Following one month, mean FEV1 increased 35.3% and 3.9% from baseline in the electro acupuncture and placebo groups, respectively. In the control group, mean FEV1 decreased by 5.8%. The between-group difference was significant ($P < 0.001$). This ascending trend of FEV1 in electro acupuncture group reached to 42.5% two years after treatment. In addition, electro acupuncture compared with placebo significantly improved ($P < 0.05$) all efficacy outcomes.

Conclusion: Electro acupuncture can stabilize pulmonary function and improves the patient's symptoms. Only a fraction of these effects can be attributed to placebo.

E2898

Use of metoprolol succinate in patients with cardiovascular diseases associated with asthma or chronic obstructive pulmonary disease (COPD)

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Objective: Assessment of safety and efficacy of metoprolol succinate in patients with cardiovascular diseases associated with asthma or COPD.

Methods: We observed 18 patients (8 females, 10 males, mean age 62.29±11.12) with mild-to-moderate asthma ($n=9$) and COPD stages I-IV ($n=9$). All the patients had comorbidity: coronary heart disease ($n=2$), arterial hypertension ($n=5$), or both ($n=11$). The patients received standard bronchodilating therapy and metoprolol (mean dose 67.19±38.15 mg/day) also indicated to these patients. To evaluate possible deterioration of bronchial conductivity (common side effect of beta-blockers) we measured FEV1 before treatment, the first day of beta-blockers administration, in 30 day and then monthly during 4 months. Furthermore, changes of clinical symptoms (degree of dyspnea, frequency of angina attacks, and blood pressure) were estimated. All the patients had 24-hour ambulatory blood pressure monitoring at baseline and in the end of the study. Exercise tolerance was evaluated by 6-minutes walking distance test (6MWD).

Results: No patient had significant ($p<0.05$) deterioration of bronchial conductivity (FEV1) during 4-month metoprolol treatment. Metoprolol effectively increased exercise tolerance evaluated by 6MWD and decreased frequency of angina attacks and blood pressure up to normal values.

Conclusions: Metoprolol succinate had no negative effect on bronchial airways in

therapeutic doses in patients with cardiovascular diseases associated with asthma or COPD.

E2899

Relatives of asthma patients: the possibility of revealing changes of the erythrocyte membrane-receptor complexes under the action of laser photomodification

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Aim: is to study possible mechanisms of laser photomodification (LPh) of erythrocyte (Er) membrane under the conditions of adrenergic and histaminergic agents action in asthma patients and their relatives.

Methods: 37 patients with atopic asthma (AA), 23 relatives of atopics (RA) and 32 healthy volunteers were analyzed. Helium-neon laser LGN-208 B ($\lambda=632.8$ nm, red spectrum) was used. The peroxide hemolysis model of lipid peroxidation *in vitro* was used.

Results: LPh decreased the inhibitory action of adrenaline on peroxide hemolysis in AA and RA. In RA (without LPh 14.9±1.29; under- 5.38±0.98; $p<0.05$) this effect was shown in a more degree than in AA (without LPh 13.25±1.51; under- 7.13±1.5; $p<0.003$) and healthy (without LPh 5.53±1.6; under- 2.07±1.25; $p<0.05$). LPh decreased the peroxide hemolysis under the action of histamin after the H2-blockade in AA (without LPh 12.98±0.9; under- 10.93±0.92; $p<0.02$) and RA (without LPh 22.47±2.02; under-12.7±1.3; $p<0.05$).

We conclude that LPh has positive training effect on Er membrane in asthma. The data obtained probably reflect the increase of beta-adrenergic and H1-histaminergic activities of Er after LPh in asthma. This method could be useful for the recognition of the adrenergic disorder in RA and is important for the evaluation of new beta2-agonists. The work was supported by Saint-Petersburg government grants M2002-4.OK-3 and PD04-4.0-102 (Certificates 302560 and ASP604079).

E2900

Disturbances of STAT6 signaling in steroid-free asthma

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Activation of the transcription factor signal transducer and activator of transcription STAT6 is critical for the differentiation of T-helper 2 cells and the production of corresponding cytokines.

The aim. The expression of STAT6, phospho-STAT6 and STAT1, phospho-STAT1 was the subject of our interest because of their crucial role in the pathogenesis of asthma.

Methods. These proteins expressed in peripheral lymphocytes, obtained from 10 subjects (5 healthy volunteers forced expiratory volume in one second (FEV1 =111,14% predicted) and 5 patients with mild atopic steroid-free asthma (FEV1=76,6% predicted), was analyzed by Western blot after the lymphocytes were lysed.

Results. The phosphorylation of STAT6 was increased in lymphocytes of asthma patients compared with healthy and correlated with the degree of airflow obstruction. STAT1 and phospho-STAT1 expression was not altered between two examined groups.

In conclusion, this study suggests that mild atopic steroid-free asthma is associated with an active T-helper 2 cell inflammatory process involving activation of signal transducer and activator of transcription 6 production.

The work was supported by Saint-Petersburg government grants: M2002-4.OK-3 and PD04-4.0-102 (Certificate ASP604079).

E2901

Molecular and cell inflammation markers in children with bronchial asthma

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The most actually problem in bronchial asthma is the searching of molecular and cell markers of inflammation.

The aim of the study was to determinate the serum dissolving antigens forms CD25, CD95, CD38, CD50 (ICAM-3), CD54 (ICAM-1) levels, as well as histocompatibility (HLA-DR) class I and II molecules and amount of T-lymphocytes in blood (positive at the same antigens) in children with bronchial asthma.

Methods: The dissolving antigens levels were measured by immunofluorescent analysis and the level of T-lymphocytes subpopulation was estimated by immunofluorescent method. We enrolled 117 children with bronchial asthma and 16 healthy controls from 7 to 14 years old.

Results: It is shown that progressing of bronchial asthma associated with the increasing of CD25⁺, CD95⁺, CD38⁺, HLA-DR⁺ lymphocytes and the decreasing of CD54⁺ T-cells, as well as the serum dissolving antigens forms CD25, CD95, CD38, CD50 (ICAM-3), CD54 (ICAM-1) levels and HLA-DR molecules level were increased compared to control ($p<0.05$). The negative correlation between the CD54 and HLA-DR blood levels and PEF50 value was determined ($r=-0.71$, $p<0.05$; $r=-0.73$, $p<0.05$ relatively) as well as between HLA-DR⁺ T-lymphocytes level and PEF75 value ($r=-0.67$, $p<0.05$).

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E2902**Effects of progressive isocapnic hypoxia on ventilatory response and respiratory center output in animal asthma model**Zhanna A. Donina. *Laboratory of Respiratory Physiology, I.P. Pavlov Institute of Physiology, St.-Petersburg, Russia*

It's known that patients with lung disease such as asthma are more frequently hypoxic than hypercapnic and airway obstruction has been shown by others to decrease ventilatory response both to hypoxemia and hypercapnia. Therefore the aim of this study was to determine whether the decreased hypoxic ventilatory response during airway obstruction is due to the low respiratory center output or mechanical abnormality of respiratory system. A rabbit breathing with resistive loads was used to test the effect of airway obstruction as does asthma. Ventilatory response (VE) to progressive hypoxia (ratio of change in VE to the change in oxygen saturation) produced by rebreathing techniques (7% CO₂, 40% O₂ and balance N₂), O₂ tension in arterial blood and diaphragmatic electromyography EMGd, a reflection of respiratory center output, were studied before and after asthma simulation. The ventilatory response to hypoxia was less with added airway resistance (with decrease in both tidal volume and frequency) than without. The maximal increment VE was 65% (P<0.05) at PaO₂ level of 43.0 mm Hg, while during unloaded breathing VE was 150% (P<0.05) at PaO₂ level of 38.3 mm Hg, in comparison with control. EMGd had increased to 117% (P>0.05) and to 142% (P<0.05) of unloaded and loaded conditions, respectively, suggesting that the respiratory center output didn't reduce and neural mechanisms involved in ventilatory response. We concluded that the decrease in ventilatory response to hypoxia in asthma simulated rabbits is related to the mechanical load applied, decrease hypoxic response may be resulted from alteration of the respiratory system mechanics due to airway resistance.

E2903**Diagnostic value of induced sputum and nitric oxide in exhaled breath condensate to control treatment of bronchial asthma**Dasha V. Kapitanova, Lyudmila I. Volkova, Valentina V. Boyarko. *Chair of Internal Diseases, Siberian State Medical University, Tomsk, Russia*

Aim: To study the value of induced sputum (IS) cytology and a nitric-oxide (NO) content in breath condensate to control treatment of bronchial asthma (BA).

Methods: IS and NO were determined in 53 asthmatics in dynamics. During BA exacerbation, the patients received budesonide inhalation suspension or prednisolon per os for 5-11 days. In remission anti-inflammatory therapy was prescribed according to degree of BA severity. 20 healthy volunteers were included in control group.

Results: In BA patients, in comparison with the control group a much greater number of eosinophils (p<0.01), neutrophils (p<0.05) and a smaller number of macrophages (p<0.05) in IS was observed. The amount of eosinophil was maximal in BA exacerbation, especially in the patients without preliminary basic therapy. In remission there was a decrease in the amount of eosinophils (p<0.01), an increase in the amount of macrophages (p<0.01). The increase in the NO content was observed in all BA patients both in exacerbation and remission, and was significantly greater in comparison with the control group (p<0.05). The greatest NO values were observed in exacerbation in the patients with severe and moderate course, especially without preliminary basic therapy. There was a negative correlation of NO and FEV₁ (r = -0.37; p<0.01). In remission there was a significant decrease in NO (p<0.01), more pronounced in the patients with mild course of BA in the background of continuous corticosteroid therapy.

Conclusion: Monitoring the IS and NO indices is informative to assess efficiency of anti-inflammatory therapy in BA.

E2904**The role of atypical pathogens in acute exacerbations of bronchial asthma**Gamal M. Agmy, Maher M. Ahmed, Shahban R. Helal. *Chest, Assiut University Hospital, Assiut, Ecuador; Pediatric, Assiut University Hospital, Assiut, Egypt; Clinical Pathology, Assiut University Hospital, Assiut, Egypt*

Setting: Assiut University Hospital.

Study Design: A serologically based prospective study.

Objective: To evaluate the role of acute infections with 4 atypical organisms in precipitating acute attacks of bronchial asthma among adults and children.

Patients and methods: Acute infections with 4 atypical pathogens were evaluated in 2 groups of patients with acute exacerbations of bronchial asthma, and compared with the corresponding rate in a matched control group. The first group of patients included 96 adults while the second one incorporated 88 children. Paired sera were tested using indirect immunofluorescent method to establish the serological diagnosis.

Results: Acute infection with Chlamydia pneumoniae was detected in 25% of adults, compared with 2% in the control group, while, acute infection with Mycoplasma pneumoniae was confirmed among 15% of adult patients compared with 3% of control group. In contrast, no evidence of acute infection with Legionella species or Coxiella burnetii could be verified among adult patients.

On the other hand, no evidence of acute infection with any pathogen of the 4 atypical organisms could be demonstrated during acute exacerbations of asthma in the children group.

In conclusion, Acute infection with either Chlamydia pneumoniae or Mycoplasma

pneumoniae has an important role in acute exacerbations of bronchial asthma among adults, while, infection with atypical organisms has no position in acute exacerbations of bronchial asthma among children.

E2905**Assessment of predictive factors for asthma exacerbations severity**Sibel Atis, Eylem Ozgur, Cengiz Ozge. *Chest Disease, Mersin University School of Medicine, Mersin, Turkey*

Several factors have been accused for asthma exacerbations, however, risk factors for severity of asthma exacerbation has not been evaluated sufficiently. We aimed to determine the predictive factors for severity of asthma exacerbation.

Retrospective analysis of data on 93 adult patients who visited our emergency department because of asthma exacerbation was reviewed. Forward logistic regression analysis estimated the strength of association of each variable with severe/very severe as compared to mild/moderate asthma exacerbation. Main independent variables were age, sex, smoking history, medication history (inhaler steroid using), compliance with medication, asthma staging according to GINA, presence of atopic diseases (rhinitis, conjunctivitis), prick test, provocative factors (respiratory tract infections, drugs), number of short-acting β -2 agonist using, number of visits to emergency department for asthma over one year, previous severe exacerbation, pulmonary functions (FEV₁, FVC, and PEF), and blood eosinophil count.

20 patients had severe/very severe (hospitalization in ICU and/or intubation because of asthma) and 73 mild/moderate asthma exacerbation. Severe asthma exacerbation was increased 1.5 fold by frequent using of short-acting β -2 agonist (95% CI:0.6-5.3, p=0.003) and 3.6 fold by in compliance with medication (95% CI:1.3-9.9, p=0.013). Also, low FEV₁ was a predictive factor for severe exacerbation (p=0.019).

In conclusion, different predictive factors, especially, frequent using of short-acting beta-2 agonist and in compliance with medication may be associated with severe asthma exacerbations as compared to milders. This suggests different mechanisms are responsible for severity of asthma exacerbation.