

30. COPD – inflammation/miscellaneous

E314

Clinical and epidemiological characteristics of chronic obstructive pulmonary disease (COPD) patients in Spain (VICE study)

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The purpose of the VICE study was to determine the clinical and epidemiological characteristics of patients with COPD in Spain.

Methods: An epidemiological, descriptive, transversal and multicentric study was carried out in primary and specialized outpatient health care centres in Spain. 2144 investigators conducting the study divided in 1826 primary care physicians and 240 pneumologists. Patients with COPD confirmed by pulmonary function tests (GOLD criteria) were consecutively included. Clinical questionnaire to evaluate the variables: age, sex, tobacco consumption, dyspnea and BMI and patients were then stratified based on the SEPAR functional classification.

Results: 10782 patients recruited and 9405 patients fulfilled the inclusion criteria and were analyzed. Clinical characteristics 67.82 ± 9.80 years; sex distribution: 80% males, 20% females; tobacco consumption: actual smokers 22.6%, past smokers: 61.4%, non-smokers: 16%; nutritional status: 23.4% with BMI < 25 Kg/m² and 24.2% patients with grade II obesity; GOLD stages of COPD severity: 33.8% mild COPD, 49% moderate COPD and 16.8% severe COPD; dyspnea grade: 0 (14.7%), 1(46%), 2(24.9%), 3(11.1%), 4(3.4%).

Conclusions: The 67% of patients with COPD had a moderate to severe pulmonary dysfunction, which implies that patients are diagnosed in an already advanced stage. Although, dyspnea is the most frequent symptom, there is a high percentage of patients without dyspnea or with minimal symptoms. Almost 25% of patients do not give up smoking. There are no changes in the percentage of females with respect to previous epidemiologic studies.

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Evaluating health care resources consumption in chronic obstructive pulmonary disease (COPD) patients (VICE study)

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This study aimed to compare the health care resources consumption according to severity of the disease and to determine the distribution of those resources

Methods: The cost analysis was carried out in Spanish primary care centres by a retrospective naturalistic study. Patients with COPD (GOLD criteria), recruited by 1826 primary care physicians and 240 pneumologists and were then stratified based on the SEPAR classification. The use of the following resources was recorded: visits to Primary Care centres and Pneumology departments, visits to Emergency rooms and hospitalizations and days of work absenteeism.

Results: 9405 patients fulfilled the inclusion criteria and were analyzed. The clinical characteristics were age 67.82 ± 9.80 years; average FEV1 55.1 ± 14.3% and mean time from diagnosis 9.69 ± 7.91. COPD severity: 33.8% mild COPD, 49% moderate COPD and 16.8% severe COPD. Those patients with severe COPD had more visits to the primary care centre than those with mild to moderate COPD (5.83, 4.65 and 3.25, respectively p < 0.001). They were also in the emergency Department more often (2.5, 1.62 and 0.9, respectively p < 0.001). Patients with severe COPD had longer hospital stays when compared to those with mild or moderate (16.7 days vs 10.9 and 8.8 days p < 0.0101) and more days of work absenteeism (51.2, 29.4 and 18.9 p < 0.001).

Conclusions: Patients with severe COPD consume more health care resources but even mild COPD patients represent a high burden for Health System. Therefore,

programs aimed to increase the awareness about the importance of early diagnosis of COPD in mild and moderate stages should result in lower costs.

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Mucociliary clearance of COPD patients

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Introduction: Border line between upper and lower respiratory tract pathology is probably artificial (especially during bronchial asthma). Also chronic obstructive pulmonary disease (COPD) is likely combined with inflammatory involvement of nasal or sinuses mucosa.

Aim: To investigate nasal mucociliary clearance of stable COPD patients (pts).

Method: Nasal mucociliary clearance was evaluated by the standard saccharine test (1mm³ particles). We calculated nasal mucociliary clearance time (NMCC time).

Material: Twenty two COPD pts (6 weeks free of exacerbation) at the age 42-81 (average 62.3yrs) were examined (10 male). According to GOLD severity: I.-10%, II.-40%, III.-31%, IV.-21%. Control group included twenty two healthy volunteers (18 male) at the age 22-72 (average 45.5).

Results: NMCC time of COPD pts significantly exceeded NMCC of control pts, median 18.90 min vs. median 9.43 min (p=0.0002). Severity of COPD (according to GOLD) had no significant influence on NMCC time (p=0.405). There was a correlation of NMCC time with increasing age (p=0.002) in the control group.

Conclusion: This research confirms, that COPD is connected with fall of nasal mucociliary clearance (COPD pts had increase of NMCC time). NMCC time of control group was age dependent. Supported by: IGA of Ministry of Health, Czech Republic NR8407-4/2005

E317

Lipid peroxidation and antioxidative enzymes in patients with COPD: relationship to pulmonary hyperinflation

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An oxidant/antioxidant imbalance is thought to play an important role in the pathogenesis of chronic obstructive pulmonary disease (COPD). The aim of our study was to assess the relationships between the degree of pulmonary hyperinflation and serum levels of the lipid peroxidation product malondialdehyde (MDA), and antioxidant capacity reflected by glutathione peroxidase (GPx), catalase (CAT) and superoxidismutase (SOD) activities in erythrocytes.

Serum levels of MDA, and erythrocyte GPx, CAT and SOD activities were measured in 138 consecutive patients with stable COPD (mean age 67±1 years). Pulmonary function tests were assessed using bodyplethysmography. Patients were divided to those with residual volume (RV) to total lung capacity (TLC) ratio lower than median value (63%) (n=70, group 1), and those with RV/TLC ≥ median value (n=68, group 2). Serum MDA levels and erythrocyte CAT activity differed significantly between group 1 and 2 (MDA: 1.9±0.1 versus 2.2±0.1 nmol/ml, p<0.05; CAT: 4.4±0.1 versus 4.9±0.1 u/gHb, p<0.02, respectively). No differences were seen in the GPx and SOD activities between the two groups. In multiple linear regression analysis, age, arterial PCO₂ and serum MDA were independent predictors of RV/TLC. We conclude that serum levels of the lipid peroxidation product MDA are linked to the severity of pulmonary hyperinflation. Supported by Ministry of Health and Ministry of Education, Slovakia.

E318

Exhaled breath condensate for evaluation of inflammation in COPD patients

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Exhaled breath condensate (EBC) continues to attract attention of researchers by its accessibility, getting material directly from lung. OBJECTIVE: To get more specific information about inflammatory process in COPD patients.

Methods: Albumin, C-reactive protein (CRP) levels, activity of alkaline phosphatase (ALP) and LDH-0 were determined in EBC of 18 COPD patients (average age 61.4±2.2 yrs) and 9 healthy control. EBC was collected on an empty stomach in the morning, then previously lyophilized and then diluted for analysis on biochemical analyzer Keysys.

Results: COPD patients had higher levels determined indices. It was observed significant difference in albumin levels in EBC between control and COPD groups (4±2 g/l and 11±1.7 g/l, p<0.025). ALP activity was determined in 11.1% cases in control, whereas in COPD patients in 68.8% (p<0.01). Analyze indices in EBC increased with growth of disease stage (GOLD, 2003). COPD patients 4 stage had higher CRP level, than patients 2 and 3 stage (0.091±0.026 g/l, 0.142±0.01 g/l,

and 0.165 ± 0.016 g/l, $p < 0.047$) and LDH activity ($p > 0.05$). Negative correlation was found between FEV₁ and albumin ($r = -0.55$; $p = 0.01$), FEV₁ and CRP ($r = -0.7$; $p = 0.002$). High inverse dependence testifies for close connection of cell pathologic changes and bronchial obstruction. The more bronchial obstruction the bigger protein fractions are in EBC as a result of cell membrane permeability changes and destruction.

Conclusion: Data show that the increasing activity of inflammatory process is associated with rise acute phase protein in EBC in COPD patients. So, EBC can provide lung disease better understanding and can be used for bronchial obstruction estimation.

E319

Neutrophil elastase in severe COPD and asthma exacerbation

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Neutrophil elastase (NE) is well-known pathogenic protease in COPD but its role is controversial in asthma.

The aim of our study was to determine the serum levels of NE in 3-4 st. COPD and severe asthma patients in exacerbation.

Methods: 18 COPD and 20 asthmatic hospitalized patients in acute exacerbation (FEV₁ < 35%) and 15 healthy controls were measured serum NE levels by a commercially available ELISA kit.

Results: Serum NE level in COPD and asthma groups was significantly higher ($p < 0.01$) than in controls. NE levels were not statistically different between COPD and severe asthmatic patients. It is worthy of note that the highest level of NE (more than 1000 ng/ml) was detected in two patients with aspirin-induced asthma.

Results

| | COPD | Asthma | Controls |
|------------------------------|---------------------------|---------------------------|-------------------------|
| FEV1 | 26.2±10.3*** | 29.5±4.0*** | 96±12 |
| Blood neutrophils (in liter) | 6.8±1.9x10 ⁹ * | 7.1±2.7x10 ⁹ * | 4.6±1.8x10 ⁹ |
| Serum NE (ng/ml) | 415±188** | 568±249** | 39±12.4 |

* $p < 0.05$ ** $p < 0.01$ *** $p < 0.001$

Conclusions: Serum elastolytic activity can play important role in severe asthma airway remodeling as in COPD.

E320

Effects of noninvasive ventilation in stable non-hypercapnic COPD

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Noninvasive ventilation (NIV) improves arterial blood gases (ABG), dyspnoea and exercise capacity in some stable hypercapnic COPD patients. Since their role in non-hypercapnic is not known, the aim of the present study was to determine the effects of NIV in COPD patients with different degrees of baseline PaCO₂. Twenty-six patients, age (mean±SD) 68±9 yr, FEV₁ 32±11%pred; FEV₁/FVC 35±11% were included and stratified into 3 groups: (1) non-hypercapnic (PaCO₂ ≤ 50 mmHg, n = 10); (2) moderately hypercapnic (PaCO₂ 51-55 mmHg, n = 8; and (3) severely hypercapnic (PaCO₂ > 55 mmHg, n = 8). NIV (BiPAP[®]) was applied 3 h·day⁻¹, 5 days a week, during 3 weeks. Spirometry, ABG, lung volumes, P_{limax}, Transition Dyspnoea Index (TDI) and the 6-min walking distance (6MWD) were measured at baseline and after 3-wk, 24-h after the last session of ventilation. Between groups comparisons were performed using one way ANOVA. Baseline values of FEV₁, FRC, dyspnoea, and the 6MWD were comparable among the 3 groups. However, improvement of lung hyperinflation, dyspnoea and exercise capacity were marginal in the non-hypercapnic group in comparison with those achieved by the moderate and severely hypercapnic patients (table 1).

Changes in respiratory function, dyspnoea and 6MWD after NIV

| Variable | Non-hypercapnic | Moderately hypercapnic | Severely hypercapnic |
|---|-----------------|------------------------|----------------------|
| Δ PaCO ₂ mmHg | -2±5‡ | -6±2 | -12±8 |
| Δ P _{limax} cmH ₂ O | 0.9±3†‡ | 9±7 | 9±11 |
| Δ FRC mL | -15±185†‡ | -804±546 | -665±394 |
| TDI points | 0.8±0.4†‡ | 4.1±1.1 | 3.8±1.3 |
| Δ 6MWD m | 16±39†‡ | 64±32 | 93±69 |

Δ = Change from baseline. Between group comparisons: † < 0.05 vs Moderate; ‡ < 0.05 vs Severe

Our data suggest that NIV application should be restricted to COPD patients with PaCO₂ greater than 50 mmHg.

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E321

Trends in healthcare utilization and costs prior to a chronic obstructive pulmonary disease (COPD) diagnosis

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This retrospective analysis evaluated trends in healthcare utilization/costs over 36 months (in 6 months increments) prior to an initial diagnosis of COPD compared to a matched control group (matched on date of diagnosis claim). A multivariate fit population-averaged panel data model was used to determine the trends for patients with COPD vs. controls.

Mean all-cause/respiratory related acute care visits significantly increased among patients with COPD from 0.33/0.07 in months 31-36 prior to diagnosis to 0.58/0.14 in months 0-6. Trends among controls over the same time period were decreasing (0.10/0.01 in months 31-36 prior to index and 0.02/0.00 in month 0-6). Mean all-cause/ respiratory related hospitalization/ER costs among COPD patients significantly increased prior to diagnosis, from \$858.36/\$314.67 (months 31-36) to \$2,368.80/\$1,300.11 (months 0-6). Again, trends among controls decreased over the same time period (\$184.25/\$29.77 in months 31-36 to \$60.14/\$12.90 in months 0-6). Total all-cause and respiratory related medical costs also significantly increased for COPD subjects over time, while decreasing among controls. All results were statistically significant in multivariate analysis.

A statistically significant increase in trends in healthcare utilization and costs were observed in this cohort of newly diagnosed COPD patients during the 36 months prior to their diagnosis, while trends in matched controls without COPD indicated decreasing utilization/costs over time. Costs and utilization for services analyzed were significantly greater for COPD subjects at all points in time compared to controls.

E322

Plasma leptin and TNF-α relation to nutritional parameters and elevated cost of ventilation in COPD patients

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An increased energy expenditure for respiration (O₂CV) in COPD patients(pts) with severe obstruction leads to relative increase in total resting energy expenditure (REE)and weight loss. Leptin (L) is a protein important in body weight regulation and is also considered responsible for cachexia in COPD pts, together with other proinflammatory cytokines, such as TNF-α.

The aim of this study is to investigate the relationships between L, TNF-α and nutritional parameters included and O₂CV

Patients - Methods: Seventeen COPD pts with weight loss > 4kg in the last 6 months (WL), 12 well nourished COPD pts (WN) and 10 age matched controls (N), all males, participated in the study. Body mass index (BMI), fat mass (FM), REE, O₂CV using an open circuit technique with dead space stimulation of ventilation, serum L and TNF-α were measured.

Results: BMI, FM were lower and REE, O₂CV were significantly increased in WL pts compared with WN COPD and N. L and TNF-α expressed per kg FM were higher in WL pts. Serum L related to TNF-α in COPD pts ($r = 0.521$, $p < 0.01$). In COPD pts serum L was correlated with BMI($r = 0.420$, $p < 0.02$), FM($r = 0.551$, $p < 0.01$) and V_{O₂}/kg ($r = -0.448$, $p < 0.02$). TNF-α was also correlated with BMI ($r = 0.349$, $p < 0.05$) and FM ($r = 0.420$, $p < 0.02$). We did not find any correlation between TNF-α and L, REE or O₂CV.

Conclusion: Circulating TNF-α levels were associated with increased L levels. L and TNF-α correlated with nutritional parameters in COPD pts, but were not responsible for the increase of REE or O₂CV in these pts.

E323

Association of airway bacterial load with serum CRP and fibrinogen in stable COPD

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Airway bacterial colonization and systemic inflammation is present in COPD patients. The acute phase proteins, C Reactive Protein (CRP) and fibrinogen are markers of systemic inflammation and associated with increased mortality. We aimed to evaluate relationships between airway bacterial load and serum CRP and fibrinogen levels in stable COPD patients.

39 patients with stable COPD and 18 healthy control subjects (10 smokers and 8 non-smokers) were studied. Neutrophil counts and quantitative bacteriologic cultures were measured in bronchoalveolar lavage (BAL), and CRP and fibrinogen levels in serum.

Mean FEV₁ was $69.6 \pm 12\%$ in COPD patients. BAL revealed the presence of microorganisms with potential pathogenicity above the established threshold ($\geq 10^3$ cfu/ml) in 61.5% of COPD and in 40% of smokers and in 12.5% of nonsmokers($p = 0.03$). COPD patients has a significantly higher total bacterial load as compared the controls (The means were 6 ± 3.4 and 2.9 ± 0.8 log cfu/ml, respectively, $p = 0.017$). BAL neutrophil count was $5.6 \pm 1.8 \times 10^9/L$ in COPD, $4.7 \pm 1.2 \times 10^9/L$ in smokers and $4 \pm 1.2 \times 10^9/L$ in non-smoker controls ($p = 0.028$). Mean CRP and fibrinogen levels were 5 ± 3.8 and 304 ± 140 mg/dL in COPD patients,

2.9±1.7 and 201±67 mg/dL in smokers, and 1.8±0.8 and 158±42 mg/dL in nonsmoker controls, respectively (one-way ANOVA, $p=0.02$ for CRP and $p=0.007$ for fibrinogen). Total bacterial load correlated with serum CRP ($r=0.52$, $p=0.007$), but not with fibrinogen in COPD patients.

In conclusion, higher airway bacterial load, serum CRP and fibrinogen levels were observed in stable COPD patients as compared to healthy non-smoker controls. The increased CRP level seems to be related to higher airway bacterial load in COPD patients.

E324

Relationship between severity of bronchial and systemic inflammation, and dyspnea, exercise performance and quality of life in patients with stable COPD

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We aimed to investigate the relationship between severity of airway and systemic inflammation and dyspnea, exercise performance and quality of life in patients with stable COPD.

35 mild to moderate stable COPD patients and 18 age-matched healthy controls were studied. Neutrophil elastase, myeloperoxidase (MPO), TNF- α and IL-8 in bronchoalveolar lavage (BAL) and CRP, fibrinogen, IL-8 and TNF- α levels in serum were measured. Dyspnea scores with Baseline Dyspnea Index (BDI), Modified Borg Scale and Visual Analog Scale (VAS), quality of life with Saint George's Respiratory Questionnaire (SGRQ), Turkish version, and exercise capacity with a 6 minute walk test (6MWT) were evaluated.

BAL MPO, IL-8 and TNF- α , and serum CRP, TNF- α and IL-8 levels were significantly higher in COPD patients as compared to controls ($p=0.03$, $p=0.0001$, $p=0.04$, $p=0.004$, $p=0.03$, and $p=0.02$, respectively). Serum IL-8 and TNF- α levels were weakly correlated with BAL levels ($r=0.3$, $p=0.05$, and $r=0.34$, $p=0.04$). BAL IL-8 levels and MPO correlated with BDI ($r=-0.37$, $p=0.04$ and $r=-0.4$, $p=0.02$, respectively), and with all scores of SGRQ ($r=0.48$, $p=0.005$ and $r=0.44$, $p=0.01$, respectively, for total score). Serum CRP correlated weakly with BDI ($r=0.32$, $p=0.03$), but not with SGRQ scores. 6MWT distance did not correlate with any of inflammatory markers in serum or BAL.

In conclusion, the severity of dyspnea and quality of life were related with airway inflammation other than systemic inflammation in patients with clinical stable COPD. Intense of airway inflammation were closely associated with the poorer dyspnea and health status, but not with the exercise performance.

E325

Could concentration of matrix metalloproteinase-9 in serum of COPD patients change into the basic disease progress and a degree of airway obstruction?

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Background: COPD is a chronic inflammatory process leading to irreversible airway obstruction. The previous studies showed that the increased level of matrix metalloproteinases (MMPs), especially MMP-9 in serum may play a crucial role in a local and systemic inflammatory process in COPD.

Study aim: 1. The estimation and comparison of sera MMP-9 concentration in COPD patients and a healthy control group.

2. The evaluation of correlation between MMP-9 concentration and a degree of airway obstruction in COPD patients.

Materials and methods: 48 COPD patients, diagnosed basing on GOLD 2005 criteria (average age 64.2 yr±10.7) and 45 healthy controls (average age 54.2 yr±9.6) were enrolled into the study. In both groups spirometry tests were performed using Jaeger system. The MMP-9 concentration in the serum taken from both group was studied using the enzyme-linked immunosorbent assay (ELISA) technique.

Results: Patients with COPD had increased levels of serum MMP-9 compared with the control group ($p=0.009$). In COPD group MMP-9 concentrations were negatively correlated with FEV1 ($p=0.003$, $r=-0.411$) and with FEV1/FVC ratio ($p=0.001$, $r=-0.349$). Not significant correlation between MMP-9 concentration and FVC was observed.

Conclusions: The results of this study show that MMP-9 may play an important role in the systemic inflammatory process in COPD. The higher serum concentration of MMP-9 is connected with the degree of airway obstruction and progression of the disease.

E327

Is there a relationship between severity of COPD and C-reactive protein (CRP) levels?

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Background: Arising number of papers deals with novel relationship between CRP levels and severity of stable COPD, but similar comparison in hospitalized (not stable) patients (pts) is still lacking.

Methods: CRP levels at the time of admission were measured in 77 consecutive hospitalized COPD pts (40 male, 37 female) and searched for their relative FEV1%, FVC%, severity of COPD according to GOLD classification, and whether the patient was hospitalized for COPD for the first time or repeatedly. The data were processed by methods of description statistics, correlation analysis and analysis of variance (Kruskal-Wallis test).

Results: Negative correlations were found between CRP levels and FEV1% ($r=-0.236$), FVC% ($r=-0.238$), both at $p<0.05$. Mean (and median) of CRP levels in mg/l were calculated in GOLD stadium as follows: st. 0:1.4(1.4), I: 7.7(5.4), II: 9.4(5.8), III: 26.2(8.1), IV: 18.5(9.1), with significance $p<0.05$ only between GOLD 0 to all other GOLD stadia. Mean (and median) of CRP were 5.2(4.8 mg/l) in first hospitalized against 23.8(8.2 mg/l) in repeatedly hospitalized pts ($p=0.058$).

Conclusion: In our study we found out significant relationships between CRP levels in hospitalized, not stable COPD pts and COPD severity expressed as spirometric parameters FEV1% or FVC%, and weak significance level as for the rehospitalization for COPD, and for GOLD stadium. These results are similar to those referred in another papers concerning the stable COPD pts.

E328

VIP (vasoactive intestinal polypeptide) and vitamin C in the serum of COPD patients before and after therapy

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VIP was determined by RIA kits from the laboratory of the Hammersmith Hospital in London, and serum ascorbate concentration was determined using spectrophotometric method. The serum level of VIP and C vitamin were measured in 40 non-smokers patients. Patients were divided into two groups. Group I included 20 patients with COPD in stable state and Group II: 20 patients with exacerbation of the disease. Diagnosis was established by clinical, roentgenographic, laboratory and lung function examinations. Laboratory analyses included blood leukocyte count, ESR and serum fibrinogen. The aim of the study was to investigate a possible neurotransmitter role of VIP on airway smooth muscle relaxation in COPD patients. Also we compared the values of serum ascorbate concentration and serum level of VIP with lung function and laboratory tests of inflammation. Spirometry in Group I patients showed: VC=2.38±0.70 l (74.45%), FEV1=1.39±0.41l(56.27%) and 100-FEV1/VC=61.39±11.92 and Group II: VC=2.17±0.81 l (64.78%), FEV1=1.28±0.43 l (52.12%) and 100-FEV1/VC=57.43±14.91. Our results showed significantly decreased serum vitamin C concentration and significantly higher serum levels of VIP in COPD patients during exacerbation before therapy compared to patients after therapy. The patients with COPD in stable state show normal serum levels of VIP and vitamin C before and after therapy.

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Prevalence of COPD in Zonguldak province of Turkey

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Chronic Obstructive Pulmonary Disease (COPD) is increasingly recognized as a leading cause of global morbidity and mortality. In this study, we aimed to investigate COPD prevalence in Zonguldak province of Turkey, located in western Blacksea region. Adult population over 18 living in central Zonguldak were enrolled to the study. They were selected according to cluster sampling methods based on regional inhabitant listings. 611 adult persons were finally enrolled to the study. They were interviewed face to face, and were given a questionnaire.

Spirometry and early reversibility testing were also performed. Of 611, 260(42.6%) were males and 351(57.4%) were females with a mean age of 49.20±15.4. 447 (73.1%) were above 40 years of age. Respiratory questionnaire, spirometry were evaluated according to GOLD criteria. COPD prevalence was found as 15.2% (n:93). Mean age in COPD group was 57.3±14.3. COPD prevalence was 17.8% in study population above age 40. GOLD stage 0 cases constituted (n:25) 4.1%. COPD prevalence was calculated as 11.1%(n:68) excluding GOLD Stage 0 cases. GOLD Stage distribution of COPD cases were as follows: Stage 0 (26.8%), Stage 1 (17.2%), Stage 2 (43%), Stage 3(11.8%), and Stage 4(1%). 79.8% of COPD patients had a smoking history. Smoking prevalence was 96.4% in male COPD patients, and 54% in female COPD patients. In conclusion, COPD prevalence is high and is an important public health problem in central Zonguldak province.

E330

The characteristics of COPD patients recently diagnosed at an outpatient clinic

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964 of one 1002 individuals newly presenting at an outpatient clinic of States Hospital for any reason in the course of 6 months and who had history of smoking at least 10 packs/year were recruited for the study and evaluated with spirometry. 452 of cases were diagnosed as COPD according to criteria of GOLD (FEV₁/FVC < %70). The spirometric evaluation of the patients with COPD was as follows: FVC: 3053±980 ml (85.2±22.9%), FEV₁:1749±729 ml (60.8±21.4%) and FEV₁/FVC: 55.9±9.5%. Assessing the patients according to guidelines of GOLD revealed that 85 cases belonged to stage 1, 223 belonged to stage 2, 141 of cases belonged to stage 3 and 3 cases belonged to stage 4. Comparison of groups with and without COPD demonstrated that statistically significant differences were noted concerning age (59.82±30.03; 49.70±13.03 years; resp. p<0.0001) (Male: 86.3%; %67) and history of smoking (42.66±29.78; 31.68±31.86)

Regarding symptoms, frequency of cough was noted similarly in both groups with and without COPD, whereas symptoms of sputum production and dyspnea were significantly increased in patients with COPD.

The most striking result with regard to spirometry/pulmonary function tests was that the patients with COPD stage 1 (4139±828ml; 114.9±15.8%) had increased FVC values compared with those of not having COPD (3577±1032ml; 99.3±20.6%). The main predictive parameters of COPD of the patients presenting the outpatient clinic were sputum production and dyspnea. 144 cases (31.85%) already had COPD stage 3 and 4 at the first visit. The increased FVC values of patients with early stage of COPD probably accounts for compensation mechanism which decreases by time as the disease worsens.

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Systemic inflammatory reactions in COPD patients

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Many studies have shown that cytokines play role in the pathogenesis of COPD. The aim of our study was to describe plasma inflammatory markers in outpatients with COPD. We studied 96 COPD patients (age – 57.8 ± 5.3), divided into 3 groups according to the stage of the disease. Measurements included clinical symptoms, spirometry and microbiology data, TNF α , sICAM and GM-CSF by ELISA.

Results are presented in table.

Table

| Groups | FEV ₁ (% pred) | TNF- α (pg/ml) | sICAM-1 (pg/ml) | GM-CSF (pg/ml) |
|----------------|---------------------------|-----------------------|-----------------|----------------|
| I gr. (n=43) | 84,3±3,2 | 7,13±2,63 | 5,76±0,55* | 2,99±0,02* |
| II gr. (n=36) | 62,7±6,8 | 8,20±2,70 | 7,83±0,61* | 2,95±0,02* |
| III gr. (n=17) | 36,5±4,1 | 9,56±2,31 | 8,50±0,69* | 3,04±0,03* |
| Control (n=12) | 108,4±6,2 | 9,99±0,77 | 3,99±0,47 | 3,17±0,04 |

*p less than 0.05 in COPD patients and control

Individual analysis showed more significant changes, particularly TNF- α , in patients with stable microbiological colonization.

In conclusion, cytokines play an important role in pathogenesis of COPD, particularly due to microbiological colonization.

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Dynamic of proinflammatory cytokines system and nonspecific markers of inflammation in patients with COPD before and after treatment with broncholitics

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The aim of our studying was to evaluate dynamic of TNF- α , IL-6, VCAM-1,

C-RP and fibrinogen in patients with COPD under the treatment with formoterol and ipratropium bromide.

Methods: We investigated 42 patients with COPD and 5 healthy persons before and after 8 weeks therapy with ipratropium bromide (160 mkg) and formoterol (24 mkg). Lung function tests and plasma levels of TNF- α , IL-6, VCAM-1, C-RP and fibrinogen were estimated.

Results: We did not get significant changes in pulmonary function tests. The level C-RP in plasma after treatment has decreased. Positive correlation between the level of C-RP and the index of smoking was found. For the whole group of patients interaction between the changes of TNF- α and IL-6 was found. Treatment with broncholitics produced the increase of IL-6 couple with TNF- α in subgroup with initially low level of IL-6, opposite to subgroup with initially high level of IL-6, in which it decreased. The most significant decrease of TNF- α as found in patients with initially elevated level of IL-6 treated with formoterol. We had found interaction between the level of IL-6 and TNF- α in smokers.

We had found interaction between the levels of VCAM1 and fibrinogen in all patients after treatment. In patients who were treated with ipratropium bromide the levels of VCAM1 and fibrinogen decreased; in subgroup of patients treated with formoterol elevation of both values was found. C-RP significantly decreased in all patients under the treatment.

Conclusion: Broncholitic treatment with ipratropium bromide and formoterol produce anti-inflammatory effect which can be proved by the IL-6 and TNF- α dynamic.

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Serum vitamin C level in patients with acute pneumonia and in COPD patients before and after therapy

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Serum ascorbic acid concentration was determined using spectrophotometric method (our reference values 30-110 μ mol/L) in 60 patients (Group I: 20 patients with acute pneumonia, Group II: 20 patients with COPD in stable state and Group III: 20 patients with exacerbation of COPD) before and after therapy. All patients were non-smokers. Diagnosis was established by clinical, roentgenographic, laboratory (blood leukocyte count, ESR, fibrinogen) and lung function examinations (VC, FEV₁ and ratio 100. FEV₁/VC were determined). The aim of the study was to compare the values of serum ascorbate concentration and laboratory indicators of inflammation in three groups of patients. Our results showed significantly decreased serum vitamin C concentration in patients with acute pneumonia and in patients with exacerbation of COPD before therapy, compared to patients after therapy (p<0.01). Laboratory indicators of inflammation are markedly increased in patients with acute pneumonia and in patients with exacerbation of COPD before therapy compared to patients after therapy (p<0.01). Also we observed negative correlation between vitamin C level and laboratory indicators of inflammation before and after therapy in patients with acute pneumonia and in patients with exacerbation of COPD. The patients with stable COPD show normal serum vitamin C values before and after therapy.

E334

The cost analysis of our COPD patients

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The cost analysis of 376 patients hospitalization in our clinic with the diagnosis of COPD between January 2005- January 2006 was evaluated retrospectively. 311 of patients were male and 65 of patients were female. The mean age of patients was 65.31 and mean hospitalization time was 9.86 days. Mean cost of medication was 392.94 USD dollars, mean cost of hospital care was 949.20 USD dollars and mean total cost was 1368.54 USD dollars respectively. The mean pO₂ value of patients of hospital entry was 54.11, while mean pCO₂ was 65.63. The accompanying diseases namely diabetes mellitus, atherosclerotic heart disease and congestive cardiac failure were found to have no effect on total cost and hospitalization time. The hospitalization time for patients with lung cancer and seckel tuberculosis were found statistically longer. The days in hospital for the patients with frequent hospitalization were unaffected while the total cost for these patients was statistically high. The antibiotic medication increased the costs and hospitalization time. Treatment in intensive care unit nasocomial infections and long term oxygen treatment both increased the costs and the hospitalization period as expected.

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COPD in Ukrainian males who were recruited for construction worksLyudmila I. Shvayko, Viktor A. Sushko, Alena S. Rjagzskaya, N. Stadniychuk.
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Aim of the study was determine resent prevalence of COPD in adult males, smokers and non smokers who were recruited for construction work.

Methods: 2.125 subjects (aged over 40, mean age: 48, 2 years) inhabitants of Ukraine, workers of building companies and nuclear industry were screened with questionnaires, spirometry, pulmonologist check-up, X-ray screening.

Results: 46, 0% of screened subjects were current smokers (mean pack/year 22.5), 13, 6% were ex smoker. COPD was firstly diagnosed in 11, 7% of persons. COPD was classified according to the GOLD classification 2003 and National Guidelines. Stage I: n=161, stage II: n=64, stage III: n=25, stage IV: n=0 cases. The screening showed low value of questionnaire, COPD diagnosed patients marked indicators significantly rarely, then during physician check-up. The most frequent indicators for COPD were age (92.4%), smoking (75.8%). Cough (31.8%) and breathlessness 12,2%, bronchial sounds were found in 10,2% of persons during physician check-up.

Conclusion: This data show underestimation of the total burden of COPD in adult males, smokers and non smokers who were recruited for object "Shelter" reconstruction and effectiveness of screening with pulmonologist check-up.

E336

Spirometric diagnosis of COPD: is postbronchodilator test reliable?Gulfidan Cakmak¹, Zuhail A. Saglam¹, Tayibe Saler¹, Esra Ataoglu¹, Mustafa Yenigun¹, Tuncalp Demir². ¹Department of Internal Medicine, 4th Internal Medicine Clinic, Haseki Training and Research Hospital, Istanbul, Turkey; ²Department of Respiratory Medicine, Istanbul University, Cerrahpasa Medical Faculty, Istanbul, Turkey

The best guidelines about COPD; GOLD and ATS/ERS, both recommend spirometric test to be performed after bronchodilator application. However, measurements after bronchodilator (BD) therapy may fail to determine borderline cases or underestimate the real stage of the disease.

Eighty-five (63M, 22F, mean age: 53.75±12.57 years) patients with a smoking history of at least 10 (mean: 35.91±27.33) pack/years, presenting to an outpatient clinic with dyspnea, cough and sputum production, were included in the study. Spirometric test was performed both before and after BD. The relationship between diagnosis and staging of COPD was assessed according to the pre and post BD values.

Before BD application, in 57 (67%) patients, FEV₁/FVC was under 70% (COPD), while post BD test revealed only 44 (52%) patients with FEV₁/FVC <70%. Thus, in 28% of cases, post-BD test failed to diagnose COPD. Moreover, in patients whose obstruction has been relieved with BD therapy, we underestimate the effect of therapy.

Staging of the cases according to GOLD with postbronchodilator FEV₁ values revealed that 11 cases had COPD stage 1 instead of stage 2 and 3 cases had stage 3 instead of stage 2. In 24.5% of cases, patients had lower stages of disease than expected. Assessment of obstruction after receiving a BD agent is somehow ironic. In fact we are either excluding the effect of treatment in those patients who can benefit from higher doses of BD therapy or failing to treat the patient efficiently while the pulmonary functions are improved with BD therapy.

In conclusion we claim that assesment of post BD test either fail to diagnose COPD in some patients or lead them to be misdiagnosed for lower stages of COPD.

E337

Smoking habit and bronchial hyperresponsiveness in patients with COPDKateryna Gashynova, Tetyana Pertseva. *Internal Medicine, DSMA, Dnipropetrovsk, Ukraine*

Aim: The aim of study was to reveal influence of the smoking habit on airway hyperresponsiveness in patients with COPD.

Study population and methods: 50 patients with COPD (Stage II) were surveyed: 14 active tobacco smokers (11 men, mean age 48.6±4.3 yrs); 12 passive smokers (10 men, mean age 50.3±3.7 yrs), who daily contact with moderate-to-heavy cigarette smokers at work or/and at home; 12 ex-smokers with no less than 1 year of abstinence and 12 non-smoking persons (9 men, mean age 49.8 ±5.4 yrs).

The baseline spirometry and provocative test with methacholine was carried out for an estimation of the airways hyperresponsiveness.

Results: All groups were similar regarding the age, gender and the duration of disease. The significant difference in baseline lung function tests was not found among the groups. Airway hyperresponsiveness was found in 71.4% of active smokers, 75.0% of passive smokers, 41.7% of ex-smokers and in 33.3% of non-smokers. The PC₂₀ among non-smoker was meanly 9.11±1.34 mg/ml, among ex-smokers - 7.31±1.26 mg/ml and they both authentically (p<0.01) exceeded a PC₂₀ in both groups of smokers. The difference between PC₂₀ for the active and passive smokers was not statistically significant (p>0.05).

Conclusion: Both active and passive tobacco smoking increase the arway hyperresponsiveness in patients with COPD in a similar extent.

Smoking abstinence no less than 1 year associates with decreasing of airway hyperresponsiveness.

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Methodological approaches to forecasting of cardiorespiratory disturbances in COPDVictor P. Kolosov, July M. Perelman. *Laboratory of Monitoring and Prophylaxis of Pulmonary Diseases, Far Eastern Scientific Center of Physiology and Pathology of Respiration SB RAMS, Blagoveschensk, Russia*

We offer technology of prognostic modelling COPD by taking into account the role of airway hyperreactivity as essential factor of development not only bronchial obstruction, but also dysfunction of respiratory muscles, mucociliar clearance etc. The given technology includes:

1. Planning of prospective research with selection of primary (formation of bronchial obstruction), secondary (progressing of obstruction, exacerbation) and end (formation of respiratory insufficiency and cor pulmonale) points of supervision.
2. Formation of a cohort of patients on the basis of a generality of key attributes of disease with use of expert system by inquiry to an electronic patients database.
3. Selection of groups of patients from total with the purpose of search of key attributes of difference.
4. Retrospective analysis of disease features with use multivariate dispersive and regression analysis.
5. Discriminant analysis with creation of mathematical models providing the maximal degree of reliability of the accepted medical decision.

Using the offered technology, we have developed prognostic models providing an understanding of ways of disease progression in the concrete patient.

In particular, to forecast the bronchial obstruction by reaction to hyperventilation with frigid air it is necessary to measure FEV₁ before and after provocation and to solve the discriminant equation: $D = 4,641 \times \Delta FEV_{1(\%)}$. Occurrence of airway obstruction in patients with a chronic nonobstructive bronchitis within one year predict at D less than -63,4.

Developed approche provides acceptance of individual programs of treatment and prophylaxis of COPD as against the standard approach focused on a degree of severity of disease.

E339

Effects of n-3 polyunsaturated fatty acids on inflammatory markers in chronic obstructive pulmonary diseaseWataru Matsuyama, Hideo Mitsuyama, Ikkou Higashimoto, Mitsuhiro Osame, Kimiyoshi Arimura. *Division of Respiratory Medicine, Respiratory and Stress Care Center, Kagoshima University Hospital, Kagoshima, Japan*

Background: Chronic obstructive pulmonary disease (COPD), which is the fifth leading cause of death worldwide, is characterized by chronic inflammation. However, no available agent can effectively cure this inflammation. Dietary supplement containing n-3 polyunsaturated fatty acids (n-3 PUFA) has anti-inflammatory effects. In this study, we hypothesized that nutritional support with n-3 PUFA rich diets maybe useful for treating COPD and we compared the clinical features and inflammatory mediator levels between the COPD patients who received n-3 PUFA rich supplement and those who received non-rich supplement.

Methods: Sixty-four COPD patients received 400kcal/day n-3 PUFA rich supplement (n-3 Group) or n-3 PUFA non-rich supplement (n-6 Group) for two years. We prospectively investigated their clinical features and measured the levels of inflammatory mediators.

Results: In six-minute walk test, dyspnea Borg scale and decreased in SpO₂ significantly improved in n-3 Group. Leukotriene B₄ levels in the serum and sputum and tumor necrosis factor alpha and interleukine 8 levels in the sputum decreased significantly in n-3 Group while, there was no significant change in n-6 Group. Two patients in n-3 Group and 3 patients in n-6 Group developed mild diarrhea, and 3 patients in n-3 Group and 3 patients in n-6 Group developed nausea, however their symptoms were controllable and they improved on treatment. Multiple regression analysis, it was proved that n-3 PUFA rich diet significantly contributed to the change in cytokine levels in this study.

Conclusion: We suggest nutritional support with n-3 PUFA rich diet as a safe and practical method for treating COPD.