Periodontal diseases have much in common with pathogenesis of other illnesses. Scientific research conducted within the recent years testifies that periodontal tissue inflammation processes are closely connected with systemic diseases; on top of that they also serve as a risk factor for the development of chronic obstructive pulmonary disease (COPD) [14]. COPD, in turn, may cause considerable extra-pulmonary systemic complications [1].

COPD is known to reduce general immunologic reaction of the body, to cause disturbance of immunologic resistibility mechanisms of all tissues, including periodontal tissues [14]. In such a case the patient’s age at the beginning of the disease is of great importance. COPD is known to develop primarily among mature and elderly individuals — after the age of 40, when the body is already going through age-related metabolic and immunological changes, and there may be mineral metabolism disorders. The following should be considered the main factors contributing to bone mineral metabolism disorders in COPD patients and influencing the course of development of generalized periodontitis: chronic inflammatory process, increased level of pro-inflammatory cytokines, hypoxia arising from progressing bronchial obstruction, development of chronic respiratory acidosis, drop in physical activity and decreased tolerance to physical exercise, administration of inhaled and systemic gluco-cortecsteroids [14, 15].

Therefore, the age-related body changes in this patient contingency overlap with COPD pathogenetic mechanisms; this fact directly influences developmental features of generalized periodontitis.

Mucous membranes of the mouth cavity are protected thanks to specific and non-specific protection mechanisms present [3, 4]. The main humoral factors of mucous membrane protection are macroglobulin (IgM), secretory immunoglobulin A (sIgA) and a number of protein and hydrocarbon compounds that include protease and antiprotease of saliva, lisozyme, lactoferrin, mucus glycoproteids [3, 4, 14]. A number of authors consider the insufficient production of antibodies, the main specific immunity defense factor, to be the consequence and integral manifestation of quantitative cell composition disorder and cell functional characteristics disorder in immungenic processes. In addition, the cells of the lymphoid and non-lymphoid line and the cytokine regulation play an important part here [8]. The cytokines generated during the inflammatory process damage periodontal tissues and cause alveolar bone resorption, which receives its clinical manifestation through symptoms of generalized periodontitis.

According to data provided by some authors, IL-1 has the most harmful impact during periodontal diseases [3, 8, 15]. Therefore, a comprehensive research of clinical symptoms of pathologic processes in periodontal tissues that would examine such local immunity performance as the level of secretory immunoglobulin A (sIgA), general protein and concentration of pro-inflammatory cytokine IL-1β in the given patient category is currently important.

The aim of the study — to research clinical and immunological features of generalized periodontitis development in chronic obstructive pulmonary disease patients via determining their periodontal status, level of pro-inflammatory cytokine IL-1β, amount of sIgA and total protein in combined saliva.

The work was carried out at the expense of the funds of the State Budget of Ukraine.

Materials and methods
63 COPD patients were examined in their remission stage (Group I), who were observed at the State Enterprise National Institute of Phthisiology and Pulmonology Named after F. H. Yanovskyi, NAMS of Ukraine. The group consisted of...
22 women and 41 men between the age of 40 and 80, (their average age was 63.8 ± 1.1 years). Forced expiratory volume over the first second (FEV₁) in all of the patients of this group before the test with bronchial spasmolytic was (46.2 ± 2.0) %; FEV₁/forced vital lung capacity (FVC) – (50.6 ± 1.6). FEV₁ after the test with bronchial spasmolytic was (48.8 ± 2.1) %; FEV₁/FVC – (51.6 ± 1.6).

Patients selection was conducted according to severity of disease as per order of Ministry of Healthcare of Ukraine dated June 27, 2013 No 555 «Unified Clinical Protocol of Primary, Secondary (Specialized), Tertiary (Highly Specialized) Medical Assistance and Medical Rehabilitation, «Chronic Obstructive Pulmonary Disease» [9]. The patients were divided into three clinical groups according to manifestation of the clinical symptoms, their functional readings and the risk of possible complications.

Control Group (Group II) consisted of 30 individuals with no COPD or any other chronic physical pathology in their medical history. Among them were 18 men and 12 women, between the age of 40 and 80, average age – (59.6 ± 1.3) years. FEV₁ (111.0 ± 3.3) %; FEV₁/FVC – (78.0 ± 0.6).

In the process of examination of the patients of Groups I and II the following methods were used: questionnaire, clinical and functional examination, periodontal examination, multislice computer tomography (MCT) of the dento-facial area, and immunological study.

The lung ventilation function test was conducted according to the spirogram data by analyzing the «flow-volume» curve of the forced expiration and general plethysmography of the body on the «Master Screen PFT» device by «Cardinal Health» (Germany). The following criteria were evaluated before and after bronchial spasmolytic: FEV₁, FEV₁/FVC ratio. The test was conducted in the morning, after a 12- to 14-hour break in taking medication. To detect a bronchial obstruction and estimate its reversibility, a respiratory function test was conducted before and 15–30 minutes after 2 inhalations (200 mkg) of short-acting β₂-agonist (salbutamol).

Dental examination was carried out by a dentist in accordance with widely acceptable methods. Periodontal examination included establishing hygienic status of the oral cavity (presence of plaque, tartar. Oral Hygiene Index (Green and Vermilion, 1960). The intensity of inflammatory process in periodontal tissues was established in accordance with papillary-marginal-alveolar index (PMA). During examination of the periodontal tissue the depth of the periodontal pockets at 6 points and the properties of the exudates were measured. Bleeding of the gums was measured against a 3-point scale according to gingival Muhammam-Cowell bleeding index. Clinical attachment loss (CAL) was estimated in mm according to the mean value between measurements at 4 points around each tooth.

Russel periodontal index (Russle PI) that, besides gums inflammation state, characterizes the extent of bone tissue destruction, was estimated in points — from 0 to 8. The degree of tooth looseness was estimated according to Miller scale as modified by Fleszar in points, from 0 to 3.

To estimate the degree of caries damage, the CFR index (caries, filling, removal) that consists of the number of corroded teeth, the number of teeth with fillings and the number of removed (or to-be-removed) teeth. The sum of these factors gives us understanding of the intensity of cariosity of a specific individual. The research results were entered into the periodontal examination card [2].

The alveolar bone height loss was examined with the use of a multi-slice computer tomography (MSCT) performed with the help of computer tomography scanner Aquilion TSX-101A «Tochiba» (Japan) with the help of free software program K-Pacs. To determine the loss of the alveolar bone, the distance from the cementum-enamel line to the top of the interdental septum (alveolar crest) was determined. The measurements were taken on the least damaged teeth where the cementum-enamel tooth line was clearly defined.

Mouth cavity local immunity study was conducted for the 63 COPD patients and 25 control group patients.

During the immunological examination the local inflammation markers – IL-1β, IgA and the total protein – were determined in the combined saliva of the patients. The combined saliva was collected in the morning on an empty stomach in order to rule out activation factors. The combined saliva was collected by spitting into a container [12]. The level of IL-1β was determined by the enzyme-linked immunosorbent assay method with the use of “CYTOKINE” commercial test system, Saint-Petersburg, Russia [5, 13]. IgA were determined by the enzyme-linked immunosorbent assay method [10] with the use of «XEMA-MEDICA» test system, Moscow, Russia [6]. The total protein was determined by the Lowry- Folin method [11], and the results were recorded in the spectrophotometer analyzer µQuant (BioTek, USA). The collected results were compared to that of the control group.

The digital research data obtained in each of the sample groups was checked and verified onto the normal distribution of values. In order to verify the normality of data distribution the Lapach S. N. et al. (2001) methodology was used (NORMSAMP-1 function integrated in Excel environment). The obtained results determined the choice of further statistical data processing method in order to verify credibility of the results [7].

Student’s paired t-test (for dependant and independent sample groups) was used to estimate credibility of differences of the average indicator values in sample groups with normal distribution. The probability indicator value (p) between the groups of lower than 0.05 was accepted as the level of probability. Wherever normal distribution was not available for calculation of the average values difference probability, Wilcoxon two-sample test was applied; its assessment was carried out by comparison against the maximum and the minimum criteria values. Alternative measurement method was used for the analysis of individual variations of the values studied.

The research results aggregation and their mathematical processing were conducted with the help of licensed software included in Microsoft Office Professional 2007 pack, license Russian Academic OPEN No Level № 43437596.

Results
As a result of the conducted research it was established that periodontal pathology and its complications took the leading role in the dental disease structure of COPD patients.
Consequently, examination of 17 (27.0 %) out of 63 Group I patients revealed total secondary adentia that developed as a complication of generalized periodontitis. These patients were using removable dentures. The other 46 (73.0 %) patients of the same group displayed a considerable loss of teeth which also required orthopedic correction.

The control group revealed no instances of total secondary adentia. Nevertheless, due to partial teeth loss and presence of tooth row defects 26 (66.7 %) out of 30 individuals examined received orthopedic treatment. This speaks of the fact that control group individuals also required orthopedic correction but to a much lesser extent.

A comprehensive examination by a dentist and consideration of the periodontal examination data as well and the MSCT revealed that 29 (46.0 %) of COPD patients were diagnosed with the I stage of generalized periodontitis and 17 (27.0 %) patients with the II stage.

All of the control group individuals also showed signs of generalized periodontitis but it was primarily of the early or I stage of severity. Thus, I stage generalized periodontitis was diagnosed in 28 (93.3 %) patients, and II stage generalized periodontitis – in 2 (6.7 %) individuals. This gave evidence to the fact that in accordance with clinical periodontal examination COPD patients revealed statistically significantly more severe periodontal defects than did individuals with no somatic pathology – 17 (27.0 ± 5.6 %) and 2 (6.7 ± 4.6 %), p < 0.001 respectively.

During the examination of COPD patients, the periodontal examination card was filled in only for the 46 individuals who had teeth at least partially, which made it possible to evaluate the appropriate criteria and fill in the periodontal examination card.

The obtained results data analysis showed that the hygienic status of the mouth cavity of the Group I patients was probably worse when compared against the control group. However, the inflammatory processes activity in periodontal tissues was probably lower in Group I patients, which was due to long-term intake of inhaled corticosteroids as part of their basic COPD medication therapy (tab.1).

Statistically significant levels of depth of periodontal pocket, recession and gum clinical attachment loss in Group I as compared to the control group individuals spoke of predominance of dystrophic and destructive processes in periodontal tissues of Group I patients. The deep periodontal pockets and significantly higher purulent discharge from dental pockets testified of poor hygiene status of the mouth cavity in COPD patients. Such periodontal tissues condition indicates increased risk of odontogenic ingress of respiratory tracts and negative impact on the development of chronic obstructive pulmonary disease.

High rate of loss of alveolar bone height and detection of tooth loosening were also evidence of increased dystrophic and destructive processes in periodontal tissues in Group I patients. Thus, in chronic obstructive pulmonary disease patients, as shown by the MSCT results, alveolar bone height loss rate was statistically significantly higher – (3.6 ± 0.1) mm, as compared to the control group (2.2 ± 0.1) mm, p < 0.001 which caused early loss of a considerable number of teeth among this patient contingency.

Therefore, it was particular to generalized periodontal disease development in COPD patients that dystrophic and destructive processes prevailed rather than the inflammatory ones in periodontal tissues, a great loss of clinical gum attachment was noted, deep periodontal pockets and considerable rate of bacterial ingress. Such periodontal tissue status was preconditioned by the fact that all the COPD patients participating in the study had been taking inhaled or systemic gluco-corticosteroids as part of their combined treatment; this served to lower inflammatory process in mouth mucus membranes.

<table>
<thead>
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<th>Table 1</th>
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<tr>
<td>Periodontal Status of Group I and II Patients</td>
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<tr>
<td>Indicator</td>
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<tr>
<td>Number of teeth in the mouth cavity</td>
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<tr>
<td>Oral Hygiene Index (Green and Vermilion), points</td>
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<td>Gum bleeding, points</td>
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<td>Tooth looseness, points</td>
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<td>Gum recession, mm</td>
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<td>Depth of the periodontal pocket, mm</td>
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<td>Gum clinical attachment loss, mm</td>
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<td>PMA index , %</td>
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<tr>
<td>PI, 0 – 8 points</td>
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<td>Purulent discharge from dental pockets, 1 – 3 points</td>
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<td>Alveolar bone height loss, mm</td>
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<td>CFR index (caries, filling, removal)</td>
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During the study of the immunological values the range margin of the secretory immunoglobulin sIgA, pro-inflammatory cytokine IL-1β and the total protein were measured in COPD patients and in the control group. The obtained data is provided in table 2.

When identifying inflammatory markers in COPD patients and in individuals with no somatic pathology of the same age and sex, a statistically significantly lower content of IL-1β was noted in combined saliva — 194,1 pg/ml (range margin 11,5 – 1681,7 pg/ml) in patients of the main group as compared to the control group individuals where IL-1β concentration was 592,7 pg/ml (range margin 27,0 – 1532,8 pg/ml), (p < 0,05) according to Wilcoxon’s U-criterion.

These peculiarities of local immunity of the mouth cavity in COPD patients were preconditioned by outstanding dystrophic and destructive processes in periodontal tissue as well as by administration of inhaled corticosteroids in the basic therapy that have considerable anti-inflammation and immunity-suppressing effect. Besides that, Group I patients displayed decreased concentration of sIgA down to 154,0 mkg/ml (range margin 10,1 – 533,0 mkg/ml) as compared to the control group individuals where the value was 211,5 mkg/ml (range margin 37,0 – 471,2 mkg/ml) (p > 0,05), which was also an evidence of suppressed local immunity on the mouth cavity in COPD patients.

Conclusion
Clinical and immunological features of generalized periodontitis development in COPD patients are prominent dystrophic and destructive processes of periodontal tissue, high rate of loss of height of the alveolar bone and detection of tooth loosening compounded by considerable loss of clinical gums attachment, deep periodontal recesses and considerable rate of microbial ingress.

Generalized periodontitis and its complications in COPD patients develop on the background of suppression of local immunity of the mouth cavity, as evidenced by the drop of IL-1β and sIgA content in combined saliva as compared to that of individuals with no somatic pathology.

Administration of inhaled corticosteroids as part of basic therapy is an additional adverse factor suppressing immunity response in COPD. On one hand the corticosteroids have an express anti-inflammatory effect, but on the other hand they suppress production of antibodies and synthesis of the necessary local defense factors.

References

КЛINIКО-ИММУНОЛОГИЧЕСКИЕ ОСОБЕННОСТИ ТЕЧЕНИЯ ГЕНЕРАЛИЗОВАННОГО ПАРОДОНТИТА У БОЛЬНЫХ ХРОНИЧЕСКИМ ОБСТРУКТИВНЫМ ЗАБОЛЕВАНИЕМ ЛЕГКИХ

Г. С. Харченко-Севрюкова

Резюме
Основными факторами, которые приводят к нарушению метаболизма, иммунологической реактивности организма и минерального обмена костей у больных хроническим обструктивным заболеванием легких (ХОЗЛ) и влияют на течение генерализованного пародонтита являются: хронический воспалительный процесс, повышение уровня провоспалительных цитокинов, гипоксия, развитие хронического респираторного ацидоза, снижение физической активности и толерантности к физической нагрузке, применение ингаляционных и системных глюкокортикостероидов, гипоксия, развитие хронического респираторного ацидоза, снижение физической активности и толерантности к физической нагрузке, применение ингаляционных и системных глюкокортикостероидов. Поэтому комплексное исследование пародонтологического статуса и показателей местного иммунитета полости рта у больных ХОЗЛ является актуальной проблемой.

Цель исследования — изучить клинико-иммунологические особенности течения генерализованного пародонтита у больных ХОЗЛ по определению пародонтологического статуса, уровня провоспалительного цитокина IL-1β, содержания sIgA и общего белка в смешанной слюне.

Объект исследования: 63 больных ХОЗЛ составили I группу, из них — 41 мужчина и 22 женщины в возрасте от 40 до 80 лет, средний возраст — (59,6 ± 1,3) года. FEV1 — (111,0 ± 3,3) %; FEV1/FVC – (78,0 ± 0,6), которые в анамнезе не имели ХОЗЛ или другой хронической соматической патологии и добровольно согласились прийти на исследование.

Контроль (II группа) состояла из 30 человек, включающих 18 мужчин и 12 женщин в возрасте от 40 до 80 лет, средний возраст — (51,6 ± 1,6) года. FEV1 — (111,0 ± 3,3) %; FEV1/FVC – (78,0 ± 0,6), которые были аналогичны не имели ХОЗЛ или других хронических соматических заболеваний и добровольно согласились прийти на исследование.

Методы исследования: анкетирование, клинико-функциональные методы исследования, периодонтологическое обследование, многоканальная компьютерная томография черепно-лицевой области, иммунологическое исследование, статистическое.

Результаты. В результате проведённого обследования установлено, что клинико-иммунологическими особенностями течения генерализованного пародонтита у больных ХОЗЛ являются выраженные дистрофично-деструктивные процессы тканей пародонта, высокие уровни микробной обсеменённости, глубокими пародонтальными карманами и значительной нестабильностью зубов со значительной потерей клинической прикреплённости.

Выводы. Установлено, что клинико-иммунологическими особенностями течения генерализованного пародонтита у больных ХОЗЛ являются выраженные дистрофично-деструктивные процессы тканей пародонта, которые развиваются на фоне угнетения местного иммунитета ротовой полости.