ISSN: 2277- 7695
CODEN Code: PIHNBQ
ZDB-Number: 2663038-2
IC Journal No: 7725

Received: 25-02-2014
Accepted: 29-03-2014

Vol. 3 No. 2. 2014
Online Available at www.thepharmajournal.com

THE PHARMA INNOVATION - JOURNAL

Mineral metabolism and pathological process of periodontal in patients with chronic obstructive pulmonary disease

L. O. Iashyna, N. I. Gumeniuk, V. I. Ignatieva, N. I Lynnyk., G. S. Kharchenko-Sevriukova

1. State Organisation "National Institute of Phthisiology and Pulmonology named after F. G. Yanovskyi, National Academy of Medical Sciences of Ukraine", Kiev, Ukraine.
[Email: diagnost@ifp.kiev.ua, Fax: +380442750568]

To evaluated the incidence of mineral metabolism and pathological periodontal processes in patients with chronic obstructive pulmonary disease (COPD).
Osteoporosis in COPD patients was detected 6 times more often than in practically healthy individuals of the same age and gender.
All patients with COPD were diagnosed with periodontal disease. In 5 (25,0%) of 20 patients with complete secondary adentia identified in 9 (45,0%) patients, generalized periodontitis and the extent and in 6 (3,0%) patients with stage II. A significant decrease in maximum density of the spongy substance of the alveolar bone in patients with COPD indicative of active manifestations of destructive resorptive processes that are related to both systemic inflammation in COPD, secondary to systemic osteoporosis or osteopenia and local factors – the loss of a large number of teeth or complete secondary adentia).

Keyword: Chronic obstructive pulmonary disease, mineral metabolism, osteoporosis, periodontal pathological processes.

1. Introduction

Chronic obstructive pulmonary disease (COPD) accompanied by related pathology is one of the greatest pressing medical and social problems worldwide. It is due to the high level of incidence, invalidization and lethality resulting both from the main disease as well as from the related pathologies. CODP leads to decrease in the quality of life and loss of labour capacity among the population. At the same time the development of COPD worsens severely when compounded with any related diseases.

Over the recent years more and more researches have turned their attention to the study of the correlation between periodontal tissue diseases and systemic diseases. It has been proven that periodontal infections may become risk factors causing the following systemic diseases: cardiovascular, respiratory tract diseases, as well as it may lead to an unfavourable course of pregnancy in women [9]. A number of studies have established a direct correlation between periodontal tissue diseases and such respiratory tract illnesses as bacterial pneumonia and chronic obstructive pulmonary disease (COPD) [7]. This may be due to the fact that through the system of blood circulation the infection from the periodontal pocket infiltrates other organs and systems, and eventually the inflammation becomes systemic. Moreover, the inflammation mediators synthesized during periodontitis also have their effect on the course of COPD. Besides, systemic diseases and their complications may in

turn have a negative impact on the pathological processes in periodontium. The hypoxic conditions arising from long-term COPD development lead to disruption of oxygen restoration processes and to periodontal tissue trophism. A number of studies have proven that COPD patients also belong to the mineral metabolism disturbances risk group [1, 5]. Occurrence of secondary systemic osteoporosis in COPD patients deserves a special mention as well as its influence on pathological processes in periodontium [3, 6].

It also should be mentioned that COPD develops mainly in patients of mature and senior age - after 40.

It has been established by a number of authors that dystrophic destructive processes in periodontal tissues as well as metabolic processes in alveolar bone crest are closely related to the structural and functional condition of a body's bone system, and to the speed of general metabolic processes and skeleton remodeling intensity [7].

The general structural and functional condition of the skeleton bones plays a key role in pathogenesis of destructive resorptive processes in periodontium. Also a high correlation has been established between the age of a patient and changes in his/her periodontal tissues and the mineral density of bones of the skeleton.

Other researchers have established a correlation between the mineral density of bone tissue and the severity of development of generalized periodontitis in pre- and post-menopausal women [4]. The works of Jeffcoat M. K. [3] identify osteopenia and osteoporosis as periodontal disease risk factors both for women and men. The decrease in mineral density of the bones may have a negative impact on the condition of periodontal tissue. Loss of skeletal bone tissue over a lifetime, bone metabolism disturbances serve to accelerate the resorptive processes of alveolar bone, which causes premature loss of teeth.

Presence of any systemic diseases, including COPD, speeds up the resorptive processes in bones significantly especially in senior persons and post-menopausal women. Therefore, a continuous loss of alveolar bone height in persons with periodontal disease is conditioned by both influence of the local pathological factors as well as general condition of the body, presence of systemic diseases [2, 7, 8]. Along with that the active destructive resorptive processes in the alveolar bone in patients with generalized periodontitis are correlated with the bone mass loss processes, bone tissue metabolism disruptions, imbalance in the remodeling process, and predominance of resorptive processes over osteosynthesis [7].

It should be mentioned that the issue of influence of metabolic disorders in the bone system on the course of periodontal diseases remains insufficiently explored in contemporary scientific literature, and the available research results appear to be contradictory. Therefore, the most reliable research method for the structural and functional condition of the bone system should be considered an examination of the mineral density of the bones [10].

Common factors of development of pathological processes include severity of periodontal systemic inflammation in COPD, severity of bronchial obstruction, reduced physical activity and exercise tolerance. Occurrence of secondary systemic osteoporosis deserves a special attention. It appears as the result of a long-term hypoxia arising during a respiratory failure, development of the metabolic syndrome, decreased physical activity in COPD patients with a severe course and receiving inhaled or systemic glucocorticosteroids [2]. Therefore, research of the pathological processes in periodontal patients with COPD is very critical.

The first such study was conducted at the SE National Institute of Phthisiology and Pulmonology named after F. G. Yanovskyi, National Academy of Medical Sciences of Ukraine.

The aim of the study - to study the incidence of mineral metabolism and pathological periodontal processes in patients with COPD.

The objects of the study were 20 patients with COPD who made up the I group (16 men and 4 women aged 40 to 80 years, mean age – (64,9±1,7) years). FEV1 before the sample with a bronchodilator – (50,1±3,5)%; FEV1/FVC – (52,8±2,6)). FEV1 after the sample with a bronchodilator – (54,8±3,4)%; FEV1/FVC – (52,8±2,7)).

The patient selection was carried out in accordance with the disease severity and

conducted under the Order of Ministry of Healthcare of Ukraine № 555 date 27.06.2013.
The control group (II group) consisted of 20 practically healthy individuals (15 men and 5 women aged 40 to 80 years, mean age – (59,8±1,5) years). FEV_1 – (115,2±4,1)%; FEV_1/FVC – (79,0±0,7)), who volunteered to participate in the study. The practically healthy individuals were men and women aged 40 to 80 years who had no history of chronic somatic diseases that would require medical supervision and treatment, and whose general clinical and functional laboratory tests were within their age norm.
Patients of the main and control groups did not differ by age and gender.

2. Materials and Methods

All patients received a clinical, periodontal examination, a study of external respiratory function (ERF), a quantitative computed densitometry (3D QCT), and a multislice computer tomography of the maxillofacial area.
Four clinical groups (A, B, C, D on the recommendations of GOLD (Global Initiative for Chronic Obstructive Lung Disease, 2011)), where the patients were attributed, were determined based on the evaluation of clinical symptoms, functional parameters and risk of possible complications.
For a comprehensive evaluation of clinical symptoms, in accordance with the GOLD 2011 Guidelines, the COPD Assessment Test - CAT (COPD Assessment Test) was used.
The study of pulmonary ventilation function of all patients was carried out according to the analysis of the "flow-volume" spirogram curve of forced expiratory volume and considering the total body plethysmography performed on "Master Screen PFT" equipment manufactured by "Cardinal Health" company (Germany). When diagnosing COPD and determining clinical groups of patients (A, B, C, D) the following parameters were evaluated before and after tests with bronchodilators: forced expiratory volume during the first second (FEV_1), the ratio of the forced expiratory volume in the first second to the forced vital capacity of the lungs (FVC) - FEV_1 / FVC. The tests were taken in the morning, after a 12-14-hour break in administration of medications. In order to determine the presence and reversibility of bronchial obstruction, the evaluation of respiratory function was performed 15-30 minutes before and after 2 inhalation sessions (200 mcg) of β_2 short-acting agonist (salbutamol).
Dental examination was carried out by a dentist with the use of conventional methods. Periodontal examination included oral hygiene assessment (presence of plaque, tartar, the Greene-Vermilion oral hygiene index). The intensity of inflammation in periodontal tissues was determined by the papillary-marginal-alveolar index (PMA). During examination of periodontal tissues the depth of periodontal pockets at 6 different points and the nature of the exudate were measured. Bleeding of gums was assessed according to the Muhlemann-Cowell index, and was measured on a 3-point scale. Rassel PI periodontal index that characterizes not only gum inflammation rate, but also bone tissue destruction rate, was assessed on a scale from 0 to 8. The degree of tooth loosening was estimated on the Miller scale in Fleszar modification, and determined on a scale from 0 to 3. Also nodes of traumatic occlusion as well as teeth and gums anomalies, denture defects were determined. Results of the examination were recorded in the periodontal assessment chart.
Examination for osteoporosis was performed on a multislice computer tomography Aquilion TSX-101A "Toshiba" (Japan) using QST Pro licensing program based on a study of mineral density of the lumbar (L_1- L_3) vertebra.
The density of the spongy substance of the alveolar bone (DAB) and the loss of height of the alveolar bone were studied with the use of multislice computer tomography (MCT), which was performed on a CT scanner, Aquilion TSX-101A "Toshiba" (Japan) using free software K-Pacs. During the study the average, the minimum and the maximum density for a given area were determined against the Hausfield scale (HU units). To determine the loss of height of the alveolar bone, the distance from enamel-cement edge to the top of the interdental septum (alveolar ridge) was measured.
Data aggregation and mathematical processing was performed with the use of licensed software products included in the Microsoft Office

Professional 2007 package, license of Russian Academic OPEN No Level № 17016297. Statistical analysis was performed with the use of mathematical and statistical features of MS Excel which employed methods of descriptive statistics. For the assessment of statistical significance of differences, parametric (Student's t-criterion) and nonparametric (Wilcoxon's T-criterion) criteria were used.

3. Results and Discussion

During the examination, the 20 COPD patients were divided into four clinical groups (A, B, C, D in accordance with recommendations of GOLD (Global Initiative for Chronic Obstructive Lung Disease, 2011)), depending on the severity of clinical symptoms, functional parameters and the risk of possible complications. In so doing 4 (20%) patients were allocated to the clinical group B, 4 patients (20%) - to the clinical group C, and 12 (60%) of the patients - to the clinical group D.

During examination of COPD patients and the practically healthy individuals of the same age and gender employing the method of quantitative computer densitometry the Z and T criteria were determined. The T-test evaluated the presence of osteopenia or osteoporosis. In this case we must note that the term osteopenia means the preclinical state of osteoporosis. The T-test results were interpreted as follows: 3,0 to -1,0 - as a norm, from -1,0 to -2,5 - as osteopenia, from -2,5 to -5,0 - as osteoporosis.

As a result of examination, systemic pathological changes in bone tissue were detected in all patients with COPD. Osteopenia was detected in 8 (40,0±11,0) % patients out of 20, and osteoporosis - in 12 (60,0±11,0)%.

Patients of the control group were diagnosed with osteoporosis only in 2 cases (10,0±6,7)%, which was significantly different from the group of patients with COPD, where osteoporosis was observed in 12 (60,0±11,0)% of patients, $p<0,01$. It should be noted that osteoporosis in the second group was detected in 2 women over 10 years in menopause. Osteopenia in the control group was identified in 11 (55,0±11,1)% of patients and in 7 (45,0±9,1)% - no changes of mineral density of the bone system were found.

The main and the control groups differed significantly in Z and T criteria. Thus, the Z-test in the first group was (-0,85±0,20), while in the second group - (0,42±0,22), $p<0,001$. The T-test in the first group was (-3,01±0,23), while in the second group (-1,44±0,21), $p<0,001$. (Table 1).

Table 1: Z and T criteria in COPD patients and in practically healthy individuals

Criteria	I Group (n = 20)	II Group (n = 20)
Z	- 0,85 ± 0,20	0,42 ± 0,22*
T	- 3,01 ± 0,23	- 1,44 ± 0,21*

Note: * - Statistically significant difference between the first and the second groups ($p<0,001$).

Analysis of these criteria in clinical groups of patients with COPD revealed the following characteristics. Patients from the clinical group D were significantly different from the practically healthy individuals by their Z, and T-criteria. Patients from the clinical group C - by the Z-criterion. While patients of the clinical group B were not significantly different from the practically healthy individuals in their Z, and T-criteria.

Based on the clinical symptoms, periodontological examination data, pantomography and MCT, all of the main group patients studied were diagnosed with periodontal disease. Besides that, a complete secondary adentia was identified in 5 (25,0%) out of 20 patients from the first group. These patients had dentures. In other patients of the same group a significant loss of teeth was observed, while during a dental examination on the basis of a periodontal examination 9 (45,0%) patients of stage I and 6 (30,0 %) patients of stage II were diagnosed with generalized periodontitis.

The control group examination revealed the following characteristics. None of the patients from the second group had a complete secondary adentia; while periodontal examination revealed catarrhal gingivitis in 6 (30%) patients, generalized periodontitis - in 10 (50,0%) patients of the I stage and in 4 (20,0%) patients of the II stage. In our opinion, the absence of apparent difference in the severity of clinical symptoms of generalized periodontitis between patients of the first and the second groups is due to the fact that all patients with COPD who took part in the study had been receiving a long-term treatment of inhaled or systemic glucocorticosteroids, which significantly reduced the inflammation of the mucous membrane of the mouth.

Measurement of height of alveolar bone was conducted only where teeth were preserved, where it was possible to differentiate the enamel-cement part

of the tooth. The loss of the height of the alveolar bone in the group I of the patients studied was (3,8±0,2) mm, which testified to a high intensity of destructive resorptive processes in the periodontal tissue. In the practically healthy control group loss of height of alveolar bone was (2,3±0,1) mm, which was statistically significantly different from the value of this indicator in patients with COPD, p<0,001.

In the study of DAB the following factors that could affect the perception of the structural and functional composition of the spongy substance of the alveolar bone were taken into account.

It should be noted that an average DAB value reflects the general structure of areas under study and does not always accurately describe the structure of the spongy substance of the bone. Therefore, for a more detailed study of the structural and functional composition of the alveolar bone a further investigation of the maximum and the minimum DAB values was conducted which provided a more detailed picture of the structure of the spongy substance in the study area. Measurements were taken in three fixed areas on the right and the left sides: Area 1 - between teeth 1 and 2, area 2 - between teeth 3 and 4, and area 3 - maxillary tuber (retromolar area), and in the case of adentia - the areas of their projection were considered (Table 2, 3).

Table 2: Density of the Spongy Substance of the Alveolar Bone and Maxillary Tuber of the Upper Jaw Bone (Hausfield scale (HU units)) in COPD Patients

Value DAB	Right Side			Left Side		
	Area 1	Area 2	Area 3	Area 1	Area 2	Area 3
Mean	367,6±46,1	388,9±46,4	108,9±34,9	488,1±56,9	428,2±47,9	138,8±39,6
Maximum	461,9±89,6	457,1±98,5	388,2±74,5*	363,9±98,2	454,7±86,2	473,9±64,7#
Minimum	- 114,7±42,4#	- 66,1±49,6#	- 216,5±56,5#	39,6±53,6#	- 40,6±47,3#	- 174,8±43,0#

Notes: * - Statistically significant difference compared to mean DAB value (p<0,05).
- Statistically significant difference compared to mean DAB value (p<0,001).

Table 3: Density of the Spongy Substance of the Alveolar Bone and Maxillary Tuber of the Upper Jaw Bone (Hausfield scale (HU units)) in Practically Healthy Individuals

Value DAB	Right Side			Left Side		
	Area 1	Area 2	Area 3	Area 1	Area 2	Area 3
Mean	387,3±44,7	361,0±40,9	183,9±41,1	447,1±35,9	403,6±44,2	193,6±56,2
Maximum	934,2±79,6#	993,8±81,1#	646,7±64,2#	998,7±68,5#	985,0±69,4#	709,0±74,6#
Minimum	- 96,4± 39,6#	- 118,0±34,5#	- 224,5±35,6#	10,3±44,0#	-82,3±37,4#	-228,3±45,7#

Note: # - Statistically significant difference compared to mean DAB value (p<0,001).

Both groups showed a significant difference (p<0,001) between the mean and the minimum DAB value in all given areas. It should be noted that in the practically healthy individuals the same significant difference was observed between the mean and the maximum DAB values in all given areas (Table 3), and in patients with COPD - in only a few areas (Table 2).

According to the obtained data, the mean and the minimum DAB values at given areas did not differ between groups I and II, however the maximum DAB value in all the areas was significantly higher in practically healthy individuals indicating a less pronounced destructive resorptive processes of the bone tissue in control group individuals compared with patients with COPD (Table 4.).

A significant decrease of the maximum DAB value in patients with COPD indicated active manifestations of destructive resorptive processes related to both systemic inflammation process in COPD, secondary systemic osteoporosis or osteopenia as well as local factors, which include full secondary adentia or loss of a large number of teeth, significantly reducing mechanical stress on the alveolar bone and contributing to the violation of structural and functional composition of the spongy substance of the bone.

Therefore, the results of the conducted study revealed that the presence of the clinical diagnosis alone does not give a complete picture of the severity of the dystrophic inflammatory processes of the periodontal tissue. Therefore, in patients with COPD in addition to a comprehensive assessment of clinical symptoms and a periodontal examination, an examination for any mineral density disorders should be conducted along with a check of density of the spongy substance of the alveolar bone.

Table 4: Maximum Density of the Spongy Substance of the Alveolar Bone and Maxillary Tuber of the Upper Jaw Bone (Hausfield scale (HU units)) in Patients of the I and II Groups

Patient Group	Right Side			Left Side		
	Area 1	Area 2	Area 3	Area 1	Area 2	Area 3
I Group	461,9 ± 89,6	457,1 ± 98,5	388,2 ±7 4,5	363,9 ± 98,2	454,7 ± 86,2	473,9 ± 64,7
II Group	934,2 ± 79,6#	993,8 ± 81,1#	646,7 ± 64,2*	998,7 ± 68,5#	985,0 ± 69,4#	709,0 ± 74,6*

Notes: * - Statistically significant difference between I and II groups ($p<0,05$).
- Statistically significant difference between I and II groups ($p<0,001$).

4. Conclusions

1. It has been proven that osteoporosis in COPD patients can be detected 6 times more often than in practically healthy individuals of the same age and gender.
2. A significant decrease of the maximum DAB value in patients with COPD indicated active manifestations of destructive resorptive processes related to both systemic inflammation process in COPD, secondary systemic osteoporosis or osteopenia as well as to the local factors, which include a full secondary adentia or a loss of large number of teeth, significantly reducing mechanical stress on the alveolar bone and contributing to the violation of structural and functional composition of the spongy substance of the bone.
3. For diagnosing of pathologic processes in periodontal tissues in patients with COPD in addition to a comprehensive assessment of clinical symptoms and a periodontal examination, an examination for any mineral density disorders should be conducted along with a check of density of the spongy substance of the alveolar bone.

5. References

1. Lehouck A *et al*. COPD. Bone metabolism and osteoporosis. Chest 2011; 139:648–657.
2. Igbal F *et al*. Declining bone mass in men with chronic pulmonary disease. Contribution of glucocorticoud treatment, body mass index, and gonadalfunction. Eur J of Epidemiology 2008; 23:115–122.
3. Jeffcoat MK, Chesnut CH. Systemic osteoporosis and oral bone loss: evidence shows increased risk factors. J of the Am Dental Association 1993; 124(11):49–56.
4. Jeffcoat MK, Lewis CE, Reddy MS. Postmenopausal bone loss and its relationship to oral bone loss. Periodontology 2000; 23:94–102.
5. Jorgensen NR, Shwarz P. Osteoporosis in chronic obstructive pulmonary disease patients. Current Opinion in Pulmonary Medicine 2008; 14:122–127.
6. Klemetti E *et al*. Mineral status of skeletonand advanced periodontal disease. J Clin Periodontol 1994; 21:184–188.
7. Linden GJ, Lyons A, Scannapieco FA. Periodontal systemic associations: review of the evidence. J Clin Periodontol 2013; 40(14):8–19.
8. Silva DR *et al*. Osteoporosis Prevalence and Associated Factors in Patiens with COPD: A Cross-Sectional STUDY. Respyratory Care 2011; 56:961–968.
9. Ghali RF. The Potential Link between Periodontitis and Systemic Diseases – An overview. J of Advanced Medical Research 2011; 1:24–35.
10. Graat-Verboon L *et al*. Whole-body versus local DXA-scan for the diagnosis of osteoporosis in COPD patients. J of Osteoporosis 2010; 640–878.