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# CLINICAL COURSE OF PERIODONTAL DISEASES IN PATIENTS WITH POSTMENOPAUSAL OSTEOPOROSIS TREATED WITH BISPHOSPHONATES

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**ABSTRACT** — The aim of the study was to assess the state of the clinical course of periodontal diseases in patients with postmenopausal osteoporosis (OP), depending on the long-term oral administration of various groups of bisphosphonates (BP). The study included 120 women aged 55–65 years with postmenopausal OP for at least three years who took complex antiosteoporetic therapy, including BP in tablet form. The dental examination included an examination of the oral cavity, the study of the pH of the oral fluid, the hygienic state of the mouth (the "Florida Probe" system). According to the results of the study, it was revealed that prolonged treatment of BP in tablets can provoke the development of inflammatory reactions in periodontal tissues. This phenomenon is associated with a shift in the pH of saliva to the acidic side, at which its buffer properties change.

**KEYWORDS** — periodontal disease, pH of mixed saliva, "Florida Probe" system, osteoporosis, bisphosphonates.

## INTRODUCTION

Osteoporosis (OP) is a group of metabolic diseases of the skeleton characterized by an imbalance in the balance of the bone remodeling cycle, which leads to a decrease in bone mass, a violation of microarchitectonics, followed by an increase in fragility and the development of fractures [10]. A large increase in this pathology was observed in postmenopausal women [10].

Many studies have been described in the literature indicating that a decrease in bone mineral density contributes to a decrease in the height of the interdental bone septum, and as a result, the dentoalveolar attachment. Therefore, postmenopausal OP is a risk factor for periodontal tissue diseases [3, 4].

The first-line drugs in the treatment of postmenopausal OP are bisphosphonates (BP), whose pharmacokinetics vary, which is associated with the characteristics of the chemical structure and reflects the degree of therapeutic doses [8, 11].

The most pronounced antiresorptive effect in comparison with other BP has intravenous administration of the substance, but at the same time the risk of developing osteonecrosis of the jaws increases [7]. Therefore, oral BP is currently the most commonly prescribed treatment in patients with postmenopausal OP [6]. They have low bioavailability, and also have a number of side effects—primarily on the condition of the upper gastrointestinal tract. [9].

Black D.M., Bauer D.C., Schwartz A.V., Cummings S.R., Rosen C.J. (2012) note that in 6–30% of cases, these drugs cause a deviation of the pH of the stomach in the acidic side [9].

At the same time, it is proved that low pH values of mixed saliva cause the development of dental diseases [9].

In 2007, A. P. Leus, associated changes in the buffer properties of the oral fluid with the values of acid-base equilibrium. When the pH drops to 6.4, the saliva becomes undersaturated with calcium and inorganic phosphate and turns into demineralizing, which subsequently causes the occurrence of caries of hard tooth tissues [5].

According to a number of authors, with a decrease in pH values, the binding property of saliva proteins with calcium increases, playing a role in the processes of demineralization. When this association is violated, calcium is deposited on the surface of the tooth, forming a supragingival tartar, which is formed by saturating the plaque with calcium phosphate crystals, which creates an obvious pathogenic factor for the development of periodontal diseases [1,2].

It was also found that the acidification of the pH of saliva secretion is the result of anaerobic processes, resulting in an increase in the activity of hydrolytic enzymes that break down carbohydrates and proteinases that ensure the adhesion of plaque and microorganisms to enamel. At the same time, the activity of acid-stable proteinases increases by 1.5 times, which is

accompanied by the appearance of periodontal tissue inflammation.

However, according to the available literature, there are not enough observations to study the development of dental diseases in patients with primary OP with long-term use of BP in tablet form. Therefore, the problem of the effect of prolonged antiosteoporetic therapy on the dentoalveolar system becomes urgent.

#### *Aim:*

to evaluate the clinical course of periodontal diseases in patients with postmenopausal osteoporosis, depending on long-term oral administration of various groups of bisphosphonates.

## MATERIALS AND METHODS

The study was conducted at the Department of Dentistry of the Central State Medical Academy of the Russian Federation from 2017–2020. The study examines 120 patients with primary OP who were treated and monitored at a dispensary for 10 years in the rheumatology department of the Federal State Budgetary Institution "Polyclinic No. 1"

**Inclusion criteria:** Inclusion criteria: women aged 55 to 65 years with diagnosed postmenopausal OP, who have been treated with BP (per os) for at least three years.

**Non-inclusion criteria:** patients with surgical menopause, malignant neoplasms, diseases of the parenchymal organs in the decompensation stage, autoimmune diseases, glucocorticoid therapy, therapy with BP for less than three years, the presence of pathological erasability (II, III degrees) of hard tooth tissues in the oral cavity, complete adentia of the dentition, secondary adentia of the teeth without orthopedic correction.

The diagnosis of osteoporosis was established on the basis of X-ray densitometry performed on the Lunar device in accordance with the Federal Clinical Guidelines for the Diagnosis and Treatment of Osteoporosis (2014).

120 patients who were on complex antiosteoporetic therapy (per os), including calcium preparations (1000 mg per day) and vitamin D (800 IU daily), depending on the BP taken, were divided into two groups:

- I — 51 women — alendronate (70 mg once a week);
- II — 69 people — ibandronate (150 mg once a month);

The comparison group consisted of 20 female volunteers aged 55–65 years without osteoporosis with chronic generalized parodontitis.

All subjects signed informed written consents to participate in the study.

The dental status was assessed after detailed monitoring of screening questionnaires, in which the patients, answering questions in detail, covered their health status, taking various medications during their life, including BP, as well as the presence of complaints from diseases in the oral cavity from the beginning of antiresorptive therapy and after three years of treatment.

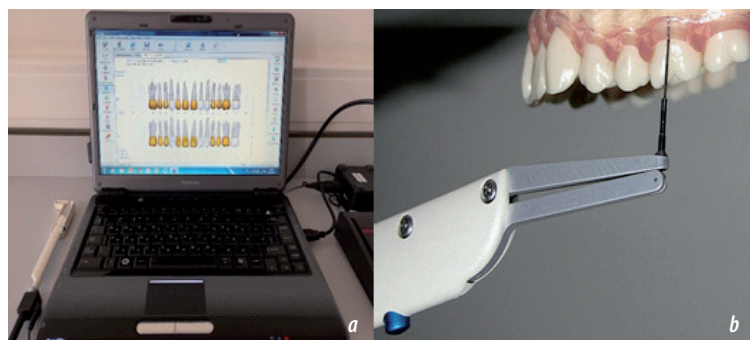
The clinical stage included an examination of the oral cavity, the study of the pH of the oral fluid, the hygienic state of the mouth (the "Florida Probe" system), as well as orthopantomography on the "Planmeca ProMax" device.

To indicate the acid-base balance, the mixed saliva was collected in the morning on an empty stomach in a sterile Petri dish ("Medpolymer" d=60 mm). Before taking the oral fluid, the mouth was rinsed with distilled water. Using a universal indicator paper ("Lach-Ner"), its pH was determined.

The diagnosis of inflammatory periodontal diseases was carried out using the "Florida Probe" system ("Florida Probe" Corporation, USA), which contains a probing device, an encoding device that generated data and, after processing them, the digital parameters were visualized on a computer screen.

Titanium dental probe with a movable tube-coupling with a diameter of 0.5 mm, provides a smooth study of clinical parameters with a constant pressure of 20 g/cm<sup>2</sup>. The program automatically determined the following indicators in absolute values: the presence of plaque, the degree of bleeding gums and the depth of periodontal pockets (with high accuracy up to 0.2 mm).

The examination procedure did not cause the patient any sharp pain and discomfort. The received information was displayed on the monitor screen with audio accompaniment and in the printed version in the form of a graphic periodontal map (Fig. 1).



**Fig. 1.** *a* — computer visualization of the periodontal map of the "Florida Probe" system, *b* — diagnostic probe

The statistical analysis of the obtained data was calculated by the methods of variational statistics with the calculation of the Student's t-test and the degree of confidence (p) using a computer and the standard software package STATISTICA 10.0 (StatSoft, Inc., USA).

## RESULTS

Monitoring of screening questionnaires revealed that the number of visits to the general dentist increased in patients with postmenopausal OP, regardless of the group and frequency of taking BP, after six months of treatment, which is associated with complaints of partial absence of teeth and periodic swelling of the gums. 93% of women noticed bleeding gums when eating solid food or while brushing their teeth, 73% — indicated the presence of recurrent caries and loss of fillings after six months of taking antiresorptive drugs.

It should be emphasized that all respondents rarely followed the standard rules for taking BF tablets (taking the drug on an empty stomach with a large amount (200 ml) of water, staying at least 1 hour in an upright position), which can be associated with the occurrence of complications from the gastrointestinal tract in the form of gastroesophageal reflux and the appearance of acidity in the stomach.

In all patients with a diagnosed OP, the pH of mixed saliva shifted to the acidic side, and the digital criteria depended on the frequency of taking BP. With weekly administration of alendronate, the acid-base balance parameter was the lowest ( $5.2 \pm 0.03$ ), in comparison with the group receiving monthly therapy ( $5.9 \pm 0.03$ ). Both coefficients significantly ( $p < 0.05$ ) differed from the control group, where the pH is within neutral values ( $7.4 \pm 0.04$ ).

Examining the hygienic state of periodontal tissues, using the device "Florida Probe", in groups I (alendronate, 70 mg weekly) and II (ibandronate, 150 mg monthly), soft plaque and hard dental deposits were detected (75% — I, 71% — II). However, the data showed no significant differences between the groups and the control.

Analyzing the data of orthopantomography, all women of group I revealed a significant uneven loss of bone tissue of the interalveolar septa within  $\frac{1}{2}$ – $\frac{2}{3}$  of the root length, which corresponded to a severe degree of periodontal disease. Mainly, the highest level of it was observed in the area of the lateral group of teeth of both jaws.

Studying the periodontograms obtained using the "Florida Probe" system, in women who took alendronate weekly (70 mg), the value of the degree of bleeding of the gums during probing was equal to

$4.6 \pm 0.04$ . Assessing the depth of periodontal pockets, the highest indicator was noted in this group and corresponded to the level of  $7.5 \pm 0.04$  (Fig. 2). Both signs were statistically significantly higher than the values obtained in women without OP with chronic generalized periodontitis.

With a monthly intake of ibandronate (150 mg) all subjects of group II were diagnosed with chronic generalized periodontitis of moderate severity. On orthopantomograms, an uneven decrease in the height of the interalveolar septa by  $\frac{1}{2}$  the length of the roots in the area of all teeth was determined.

Examining the indicator of the degree of bleeding of the gums in women who were on monthly treatment, its average value was established ( $3.1 \pm 0.03$ ). Against this background, the digital values of the depth of the clinical pocket were —  $4.78 \pm 0.03$ . As an example, Fig. 3 shows a periodontal chart of patient B. 61 years old, who took ibandronate for more than 3 years.

## DISCUSSION

Long-term use of complex antiosteoporotic therapy reduces bone resorption by suppressing the activity of osteoclasts, which leads to an increase in bone mineral density, but at the same time, long-term use of BF in tablet form has negative sides: it can provoke the development of an inflammatory reaction in periodontal tissues, despite systematic observation by a dentist.

This phenomenon is associated with a shift in the acid-base balance of saliva to the acidic side, at which its buffer properties change.

As a result, the progression of periodontal pathology was observed. We believe that statistically significant changes in the periodontal status of patients who took BF are also associated with an increase in the virulence of the periodontal flora in an acidic environment. All of the above correlates with the authors' data indicating the relationship between the development of dental diseases with a decrease in the pH of the mixed secret and a change in its protective functions [1, 2, 5]

It should be particularly noted that women who received weekly therapy with alendronate (70 mg) were in a more unfavorable situation compared to patients with monthly ibandronate (150 mg). According to our data, the degree of gum bleeding during probing was 1.5 times more pronounced and the depth of periodontal pockets was 1.6 times more pronounced (Fig. 4, 5).

## CONCLUSION

According to the results of the study, the highest risk of an active course of inflammatory periodontal

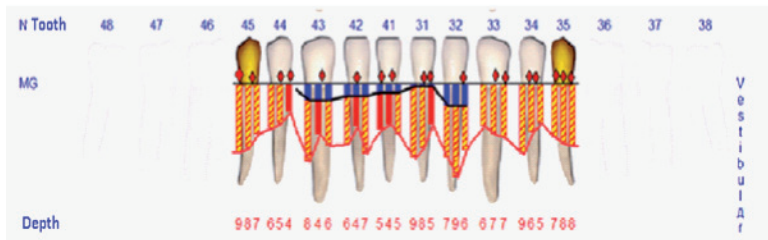
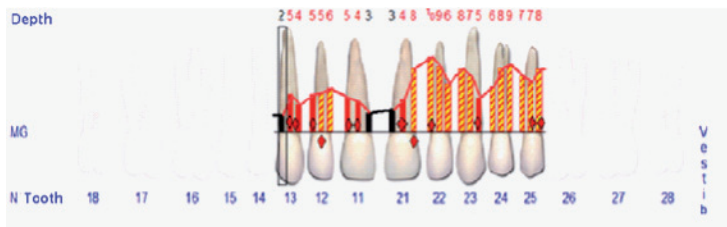


Fig. 2. Periodontal chart of patient B. 61, treated with ibandronate for more than 3 years

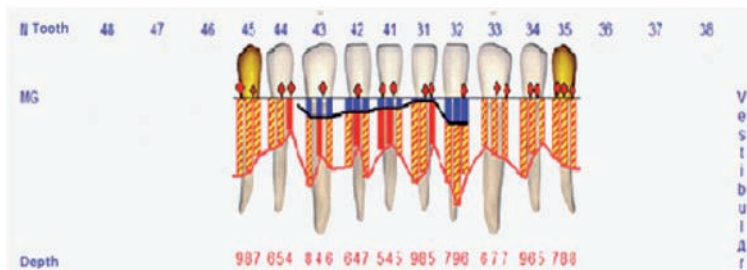
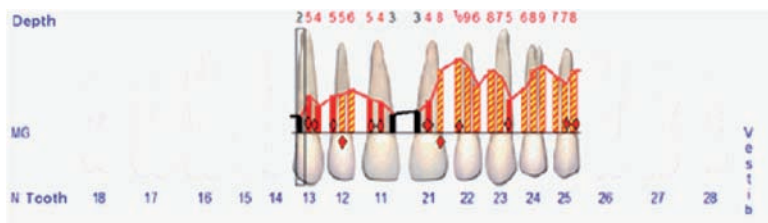


Fig. 3. Periodontal chart of patient B. 61, treated with ibandronate for more than 3 years

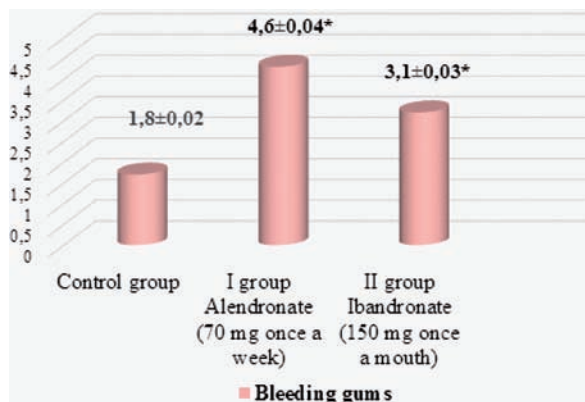


Fig. 4. Comparative assessment of the values of gum bleeding in patients of the control, I and II groups  
(\* — the indicators have statistically significant differences with the data in patients with OP and normal bone mineral density), ( $p < 0.05$ ))

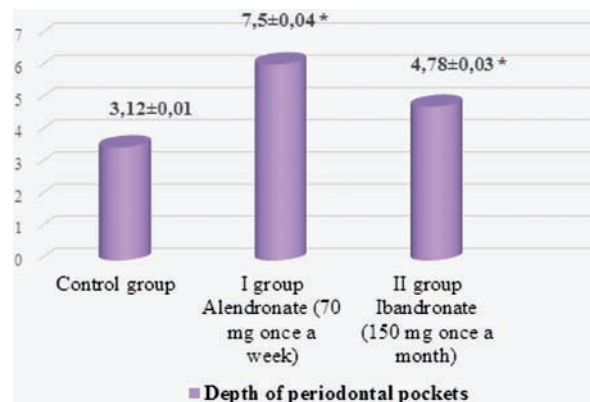


Fig. 5. Comparative assessment of the depth of the periodontal pocket in patients of the control, I and II groups who took BP  
(\* — the indicators have statistically significant differences with the data in patients with OP and normal bone mineral density), ( $p < 0.05$ ))



pathology is exposed to persons who take weekly tablet forms of alendronate 70 mg. It should be recommended that patients visit a dentist every three months in order to register the condition of periodontal tissues for preventive and therapeutic measures.

Important in the interdisciplinary interaction is the mandatory referral of women with postmenopausal OP, receiving BF, to the dentist to assess the monitoring of the state of the dental system.

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