

Correction of disordered mineral bone metabolism in patients affected by chronic periodontitis

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Abstract

One of the main mechanisms in pathogenesis of chronic periodontitis is disordered bone metabolism that is accomplished by cortical plate's resorption, destruction of the interdental septums and osteoporosis of the jaws. Administration of osteotropic agents will allow achieving efficient results in treatment of the patients affected by periodontal disorders, lower the tendency of bone resorption and stimulate the processes of regeneration.

The article demonstrates the results obtained after the surgical treatment of the patients with osteopenia affected by chronic periodontitis of II–III degree that were administered simultaneously with synthetic osteoplastic material Tricalcium phosphate and a bone resorption inhibitor Ibandronic acid. It has been established the high efficiency of the recommended treatment that was proved by positive progress of biochemical markers of bone metabolism in blood serum and urine of the individuals from the main group taken 24 month after the beginning of the treatment. The study shows that the rise of osteocalcin by 11,5% in the blood serum of the main group patients 2 years after the research and the amount of desoxypyridynolin, on the other hand, was by 21,72% lower comparing with those from the main group ($p < 0,05$).

Keywords

bisphosphonates, bone tissue, chronic periodontitis, synthetic osteoplastic material

Introduction

A number of studies have proved that periodontal disorders of inflammatory nature are the most frequently affecting people world wide and there is no tendency to decline. According to Beck and Slade (1996) more than 25% of all examined patients with symptoms of periodontal inflammation between the ages of 35 to 44 years also demonstrate symptoms of periodontal distraction. Periodontal disorders is one of the most complicated problem in stomatology and despite the achievements in this field

on the whole, the number of the patients remains significant and the disease itself leads to the tooth loss.

Risk factors for periodontal disease can be classified as local and general. A part from local factors, there are general risk factors for periodontal disease that may have a genetic basis within certain inherited conditions with periodontal manifestation. The findings provided by Malyj and Antonenko (2013) demonstrated that there are also metabolic, hematological, endocrine, nerve-somatic (rheumatism), cardiovascular, blood disorders, vitamin deficiency, infection diseases, obesity, gastroenterological

and breathing disorders and environmental risk factors within the general category as well as metabolic osteopathy-osteopenia and osteoporosis.

The data introduced by Offenbacher (2016) show changes of the jaw's bone tissues in pathogenesis of generalized periodontitis. Dystrophic-destructive processes in periodontal tissues, bone metabolism of the jaws are tight connected with structure-functional state of the bone system and also with the metabolic activity and the intensity of inner remodeling of the skeleton.

According to Page (1991) the low density of the bone structure in form of osteopenia can be considered as a predictor in development of attachment loss (including inflammation), increased bone remodeling and as a result-resorption of the inter-dental septums, alveolar bone itself and disturbances of the bone formation.

Among the osteopathy that might influenced periodontal pathology is osteoporosis-systemic bone defeat. The statistic introduced by WHO suggests that the prevalence of osteoporosis is on the growth and ranks fourth after the cardiovascular disorders, oncology and diabetes. According to a number of scientists, this disease causes not only disordered boneskeleton metabolism but also affects the jaws with alveolar processes. The statistics suggested by Reddy (2011) illustrated that chronic generalized periodontitis is diagnosed in 40% of those affected by osteoporosis and in contrast, there are only 12,5% cases of this disease in patients not affected by osteoporosis. Domination of bone resorption on osteo-regeneration inevitably leads to the damage of the periodontal support, development of inflammatory-destructive processes, tooth loss and disorganization of dento-jaws system in general. The occurred disordered bone metabolism of the skeleton that was initiated by different etiopathological factors and is age and gender related can cause inflammatory-dystrophic processes in the jaws and produces remodeling of alveolar processes. Besides, Netyuchailo and Ishcheikina (2014) indicated that these abnormalities might activate oral pathogenic microflora that could prove to become very aggressive.

The increased prevalence of chronic generalized periodontitis strongly recommends a complex treatment. The flap surgery with better access for root cleaning and excision of the infected connected tissues remains central. More recently, a combination of osteoplastic materials introduced into bone defects have also been found to be effective. Multiple investigations performed by Lychota et al. (2012) demonstrated the advantages of surgical management combined with osteoplastic materials for stimulation of periodontal reparation.

Thus, it can be summarize that changes in the bone tissue in case of chronic generalized periodontitis require additional interference directed towards inflammation in suspensor dental apparatus by administration of osteotropic therapy to normalize disordered bone metabolism, suppress bone resorption and stimulate bone formation.

Materials and methods

There were examined 90 persons between the ages of 31 to 69 years diagnosed with chronic generalized periodontitis of II and III degree affected by osteopenia. The flap surgery was recommended for the patients as a part of the complex treatment together with administration of recommended pharmacological agents. The written permission from the patients was attained. The research excluded people with somatic diseases at the stage of decompensation, malignant tumors, infection diseases and decompensative diabetes. All patients were divided into the main and control groups randomly chosen by age and sex. Flap surgery by Cishinskyy-Vidman-Neuman was performed in patients of both groups. Patients from the main group were appointed with osteoplastic material Tricalcium phosphate and bone resorption inhibitor Ibandronic acid administered by 1 tablet 150 mg taken ones a month at the same day over the course of 3 month. The tablet should be taken without chewing and swallowed with a glass of drinking water (180–240 ml) at sitting or staying position.

Tricalcium phosphate is an osteotropic material 100% synthetic that does not contain any other products such as proteins, prions and other protein fractions. Porosity of the material causes formation of osteonin mature bone tissue on the surface of the granules. Ibandronic acid, on the other hand, is an agent from the group of bisphosphonates.

During the postoperative period all patients from both main and control groups were appointed with pharmacological therapy: Azithromycin 500 mg taken for three days (dosage per course 1,5 g), Loratadine 10 mg ones a day for 10 days.

The comparison of the results gained by biochemical investigation was conducted between a group of 30 healthy individuals that did not have any periodontal disorders and did not have general somatic pathology.

Efficiency of the recommended treatment was assessed by analyses of structure-functional state of the bone tissue using biochemical determination of the markers of bone metabolism: osteocalcin (OC) in blood serum and desoxypyridynolin (DPD) in urine.

For biochemical examination the blood was collected from the vein in the morning before breakfast (from 9 am to 10 am) in laboratory and was examined immediately. The quantities determination of osteocalcin in blood serum was provided by immune-enzyme test Nordic Bioscience Diagnostics A/S N-MID Osteocalcin ELISA (Dannemark). The level of desoxypyridynolin (DPD) in the morning urine was measured by using immune-enzyme method with "Metra DPD EIA kit" (Quidel Corporation, USA) by correlation with contain of creatinine (Cr).

Markers of osteoporosis in blood serum and urine were calculated 12 and 24 month after the study.

According to the requirements of bioethics there are written permissions of the patients for examination of biological materials.

The time of the research lasted 24 month.

Results

The results of laboratory investigation conducted before the research have proved that there is a certain decrease of OC in 1,6 times in blood serum of the patients from the main and control groups in comparison with healthy individuals ($p < 0,001$). The biochemical indicators before the treatment and progress of their changes after the appointed treatment in people affected by chronic periodontitis and osteopenia are demonstrated in Table 1. Concentration of desoxypyridynolin (DPD) in main and control groups before the research was ($6,16 \pm 0,54$) nmol/mol/Crand ($6,38 \pm 0,44$) nmol/mol/Cr respectively and was in 1,8 times higher than in healthy people ($3,43 \pm 0,13$) nmol/mol/Cr ($p < 0,001$).

It has been proved that 12 month after the introduced treatment there was a significant increase of osteocalcin (OC) in blood serum of the main group in 1,6 times ($p < 0,001$) up to ($28,62 \pm 1,62$ ng/ml) comparing to the initial data. Moreover, the difference between OC in the main group and healthy group after the therapy was unreliable ($p > 0,05$). In control group, on the other hand, patients have had only surgical interference without osteotropic and anti-resorption therapy and OC has raised also in 1,4 times according to the initial statistic ($p < 0,001$). However, its concentration in blood serum of the control group appeared much more lower ($p < 0,01$) than in healthy individuals. Furthermore, 24 month after the treatment there was a further growth of the amount of OC in the main group by 37,2% comparing to initial level ($p < 0,001$). Concentration of OC in the blood serum of control group was ($26,02 \pm 1,87$ ng/ml) two years after the treatment and was considerable lower than in healthy people ($p < 0,05$).

The marker of the bone resorption DPD in urine experienced also considerable changes after the treatment in the main group demonstrating a decline in 1,5 times in contrast to the initial level ($p < 0,01$). Despite the fact that DPD had decreased in 1,3 times in control group over the period of 12 month comparing to initial level ($p > 0,05$), it proved to be much more higher than in healthy individuals ($3,43 \pm 0,13$ nmol/mmol Cr). The marker DPD in urine of the main group had declined over 24 month since the research by 39,1% as for beginning ($p < 0,01$) and was ($3,75 \pm 0,68$ nmol/mmol Cr). There was a fall only by

24,9% of DPD in control group over the indicated period by comparison the end and the beginning ($p < 0,05$).

In conclusion it should be summarized that the recommended surgical interference together with administration of osteoplastic material Tricalcium phosphate and a bone resorption inhibitor Ibandronic acid have promoted significant positive effect of biochemical characteristics in patients affected by generalized periodontitis and osteopenia in contrast with the control group.

Discussion

The results gained by laboratory investigations of the blood in patients affected by chronic generalized periodontitis with osteopenia taken before the treatment show the decreased amount of osteocalcin in comparison with healthy people. Concentration of osteocalcin in blood demonstrates a metabolic activity of osteoblasts. The significant decrease of osteocalcin in blood indicates, in my opinion, decreased contain of Calcium in blood serum that enhances chances of osteopenia with disturbed bone formation. According to Otomo-Corgel et al. (2012) the reduction of calcitonine can indicate development and progression of osteopenia and other osteopathy in patients with periodontitis and also might be used for early diagnosis of the disease as well as being considered as a risk factor.

There were also expressive changes of desoxypyridynolin in patients with generalized periodontitis and osteopenia before the surgical interferences. Desoxypyridynolin has increased in urine ($p < 0,05$) in all patients in comparison with healthy people. Kuznyak et al. (2015) suggested that significant concentration of desoxypyridynolin urine exhibit the metabolic activity of osteoclasts and its increase, on the other hand, indicates the bone resorption and might lead to osteopenia.

The restoration of the damaged or lost bone tissues remains very important in modern maxilla-facial surgery as there are many diseases affected by the destruction of the hard bone tissues such as radicular cysts, benign bone tumors and many others.

Administration of osteotropic agents in patients with periodontal disorders enables to achieve efficient results, arrest the lost of the bone tissues of the jaws and stimulate regeneration. The findings provided by Bandrivsky

Table 1. Biochemical markers of bone metabolism before treatment and dynamic of changes after the recommended treatment in patients with chronic generalized periodontitis.

Biochemical markers	Main group (n = 30)			Control group (n = 30)			Healthy group (n = 30)
	Before treatment	12 month after treatment	24 month after treatment	Before treatment	12 month after treatment	24 month after treatment	
Osteocalcin, ng/ml	18,46 ± 1,23 ^{ooo}	28,62 ± 1,62 ^{***}	29,39 ± 1,65 ^{***}	18,34 ± 1,44 ^{ooo}	25,52 ± 1,62 ^{***o}	26,02 ± 1,87 ^{***o}	30,43 ± 0,74
Desoxypyridynolin, nmol/mmol Creatinine	6,16 ± 0,54 ^{ooo}	4,09 ± 0,53 ^{**}	3,75 ± 0,68 ^{**}	6,38 ± 0,44 ^{ooo}	5,04 ± 0,64 ^o	4,79 ± 0,63 [*]	3,43 ± 0,13

Note:

* – between the indicators before and after treatment within the group * – ($p < 0,05$); ** – ($p < 0,01$);

o – between the indicators before treatment and the indicator of a healthy group; ° – ($p < 0,05$); °° – ($p < 0,01$). °°° – ($p < 0,001$).

(2013) demonstrated that the complex treatment of the patients with generalized periodontitis and osteopenia can eliminate the source of inflammation, arrest bone resorption and provide an extended stabilization in periodontal tissues. The findings of the authors (Boicanyuk 2013; Georgiev 2013; Shtenberg 2014) suggested that the synthetic agents have many advantages for this purpose among the others materials. Masur and Leonenko (2013) considered bisphosphonates as the pharmacological agents of the first line in management of osteopenia and osteoporosis.

As can be seen from the results, proved by biochemical investigation, the recommended treatment that includes flap surgery together with administration of osteoplastic material Tricalcium phosphate and a bone resorption inhibitor Ibandronic acid have positively influenced osteogenesis. The patients from the main group demonstrated positive dynamic of osteocalcin and desoxypyridynolinin comparison with analogical data in patients from the control group.

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Conclusions

Development of chronic generalized periodontitis of II and III degree in patients with osteopenia is characterized by significant changes of the bone metabolism markers. There was a decrease of OC by 39,5% and an increase of DPD by 45,1% in patients from the main and control groups in comparison with healthy people ($p < 0,001$).

The recommended treatment with synthetic osteoplastic material Tricalcium phosphate and a bone resorption inhibitor Ibandronic acid has proved to be efficient to enhance osteogenesis and suppress bone resorption that is reflected in results of biochemical investigation: concentration of OC raised by 37,2% and DPD decreased by 39,1% after 24 months in ce the beginning of the research comparing to the initial data ($p < 0,01$).