

# Influence of Zinc Picolinate on Osteoregeneration and Mineral Metabolism in Patients with Periodontitis and Application of Titam Implants

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## Picolinat de zinc: corecția proceselor osteoregeneratoare la pacienții cu parodontită și aplicatori ai implanturilor din titan

Picolinatul de zinc posedă proprietăți osteoregeneratoare pronunțate care se manifestă prin stimularea activității fosfatazei alcaline termolabile în oase și prin creșterea raportului activității fosfatazei alcaline termolabile și a fosfatazei acide tartratrezistente. În parodontită se relevă dereglări nesemnificative ale metabolismului fosfo-calcic; conținutul de Fe și Zn scade în stadiile avansate ale parodontitei. Picolinatul de zinc manifestă efecte favorabile asupra modificărilor metabolismului mineral provocate de parodontită. Cercetările efectuate confirmă perspectiva utilizării picolinatului de zinc în calitate de remediu eficient de corecție a dereglărilor metabolice provocate de parodontită.

**Cuvinte-cheie:** parodontită, corecția metabolismului, picolinat de zinc.

## Пиколинат цинка: коррекция остеорегенераторных процессов у больных пародонтитом с аппликаторами титановых имплантатов

Пиколинат цинка обладает выраженными остеорегенеративными свойствами, которые проявляются стимулированием активности костной термолabile щелочной фосфатазы и соотношения между активностью термолabile щелочной фосфатазы и тарtrat-резистентной кислой фосфатазы. Пародонтит вызывает несущественные изменения в фосфорно-кальциевом обмене, а содержание железа и цинка снижается только в поздних стадиях заболевания. Пиколинат цинка благоприятно влияет на изменения минерального обмена, вызванные пародонтитом. Проведенные исследования подтверждают перспективу использования пиколината цинка в качестве эффективного средства для коррекции метаболических изменений, вызванных пародонтитом.

**Ключевые слова:** пародонтит, коррекция метаболизма, пиколинат цинка.

### Introduction

Investigations devoted to the study of biochemical aspects of periodontitis and remedies for its treatment have particular importance for medical science [1]. Research in recent years towards the study of etiologies and physiopathology of periodontitis, have led to various changes in the homeostatic system and disease evolution, programs had been developed and diagnostic tests to determine disease trends and forecast, new treatment programs were proposed [3, 4, 10, 11]. At the current level of knowledge, however, many issues remain undecided or still insufficiently elucidated in this disease. Far from being solved are the complex problems of diagnosis of homeostatic changes, the development of new therapeutic programs and optimizing methods of the characteristic metabolic changes of such diseases. Currently there are attempts to find effective remedies with osteoregenerative effect in experimental osteoporosis [7].

Bone is a dynamic system which is permanently renewed during a person's lifetime by the remodeling process: osteolysis – bone resorption and osteogenesis – bone formation. The aforementioned processes take place in certain bone structures called basic multicellular units (BMU). Bone mass depends on the balance between processes of bone resorption and formation by the number of BMU activated in a given time interval and systems bone segment. Biochemical markers of bone metabolism can provide information about the intensity of metabolic processes in bone tissue and in particular, the

activation frequency of BMU.

Alkaline phosphatase, which is secreted by the osteoblasts and catalyses the hydrolysis of organic esters of phosphoric acid, is currently the only enzyme with practical significance for bone tissue pathology. In blood serum three isoenzymes of alkaline phosphatase are present: liver, kidney and bone. Bone isoenzymes differ from the hepatic alkaline phosphatase by a greater susceptibility to heat inactivation. Bone thermo stable alkaline phosphatase is an enzyme located on the osteoblasts membrane.

Acid phosphatases are a group of lyzosomal enzymes which hydrolyze monophosphoric esters in acid medium. They are present in bone tissue, macrophages, platelets, red blood cells, spleen etc. Bone acid phosphatase isoenzyme detection is based on its property to preserve activity in the presence of tartrate. Tartrate resistant acid phosphatase is released by osteoclasts during the adhesion with the brush edge of the cell to the bone, when a number of lyzosomal enzymes are eliminated, which degrade organic components of bone.

Calcium phosphate salts play an important role in bone metabolism. They represent 95% of the inorganic composition of bone. They are presented in a form similar to hydroxiapatite – a mineral frequently found in nature – and therefore are considered to be salts of hydroxiapatite type (*hydroxiapatite like salts*) [2, 4]. In conjunction with these two basic elements of bone tissue – calcium and phosphate, zinc is also present which increases inorganic phosphate uptake. Microelements show significant action on the state of bone, activating alkaline

phosphatase, primary osteogenetic enzyme [8, 10]. Also, zinc manifests stabilizing action on the cell membranes preventing the release of hydrolytic enzymes, which control bone tissue degeneration speed [7, 11].

Coming from the above, the purpose of this study was to assess changes of the activity of key markers of bone metabolism – termolabile alkaline phosphatase and tartrate resistant acid phosphatase, as well as some indices of mineral metabolism (Ca, P, Fe, Zn) in patients with periodontitis and the opportunity to introduce Zn picolinate into periodontitis treatment protocols as a pathogenic remedy for the correction of metabolic disturbances specific for the condition.

### Material and methods

Research trials were conducted in the Clinic of the Pediatric Dentistry Department of USMF “Nicolae Testemitanu”.

To research the influence of zinc picolinate on main bone metabolism markers – termolabile alkaline phosphatase (FAT) and tartrate resistant acid phosphatase (FATR) and indices of mineral metabolism in patients with periodontitis, 27 patients with chronic generalized periodontitis of moderate severity and impairment were selected. Participants were aged between 30 and 70 years with disease duration greater than 10 years. Treatment (standard treatment) of chronic generalized periodontitis was performed according to contemporary protocols including antimicrobial remedies, anti-inflammatory drugs, antiseptics and orthodontic treatment with application of titanium implants (after professional oral hygiene, curettage of periodontal bags, selective polishing etc.) [8, 9].

Patients were divided into 2 groups:

I – patients (12) which have received traditional complex treatment (standard treatment);

II – patients (15) undergoing standard treatment including zinc picolinate (study group).

Total alkaline phosphatase and total acid phosphatase activities were determined using standard sets of reagents (Elitech, France). The method is based on the ability of the enzyme to hydrolyze p-nitrofenilphosphate to p-nitrophenol, which is determined using spectrophotometrically.

Bone termolabile alkaline phosphatase is calculated by determining the difference between total alkaline phosphatase activity and the thermo stable alkaline phosphatase activity. To determine thermo stable alkaline phosphatase, the serum is subject to a preincubation heating at 56 °C for 10 minutes. The assay for the bone tartrate-resistant acid phosphatase activity, is the same as for the thermo stable alkaline phosphatase, with the exception that it takes place in acid medium in the presence of the inhibitor – potassium-sodium tartrate (1 mol/l concentration).

Assays for total calcium, inorganic phosphate, iron and zinc levels in blood serum were performed by photometric method using standard sets of reagents (Elitech, France).

### Results and discussion

The study showed reduced activity of total alkaline phosphatase and its termolabile isoenzyme in the blood serum in patients with periodontitis (Table 1). Thus, until the beginning of the treatment both total alkaline phosphatase activity and the termolabile alkaline phosphatase in blood serum were reduced by 24% and 31% (p < 0,05) respectively in comparison with control levels. In patients undergoing standard treatment including zinc picolinate (study group), there is a continuous increase in the activity of mentioned enzymes up to the levels in the control group, which were higher than the initial values. Thus termolabile alkaline phosphatase activity after 6 and 12 months of treatment increased by 66% and 54% respectively from the initial indices at the beginning of the treatment. Increased levels of termolabile alkaline phosphatase activity

Table 1

Dynamics of biochemical markers of bone tissue metabolism in blood serum of the patients with periodontitis with the application of titanium implants and zinc picolinate administration

Research conditions	nr.	Total alkaline phosphatase (UI/l)	Termolabile alkaline phosphatase (UI/l)	Total acid phosphatase (UI/l)	Tartrate-rezistent acid phosphatase (UI/l)	K ration
control	20	283,9 ± 20,7 (100 %)	17,12 ± 1,64 (100 %)	1,02 ± 0,16 (100 %)	0,83 ± 0,06 (100 %)	20,6
<b>standard treatment</b>						
Baseline	12	215,8 ± 12,6* (76 %)	11,75 ± 1,40* (69 %)	0,89 ± 0,12 (87 %)	0,66 ± 0,07 (80 %)	17,8
6 months	8	243,2 ± 25,3 (86 %)	13,90 ± 1,23 (81 %)	0,95 ± 0,81 (93 %)	0,81 ± 0,08 (98 %)	17,2
12 months	6	249,8 ± 27,4 (88 %)	12,84 ± 1,36 (75 %)	1,05 ± 0,78 (103 %)	0,85 ± 0,09 (102 %)	15,1
<b>standard treatment + zinc picolinate</b>						
Baseline	15	213,6 ± 16,8* (75 %)	11,80 ± 1,10* (69 %)	0,93 ± 0,12 (91 %)	0,71 ± 0,08 (86 %)	16,6
6 months	13	354,2 ± 26,7# (125 %)	21,9 ± 1,23*# (128 %)	0,79 ± 0,08 (77 %)	0,57 ± 0,07* (69 %)	38,4
12 months	8	329,8 ± 28,6# (116 %)	20,14 ± 1,81# (118 %)	0,82 ± 0,074 (80 %)	0,64 ± 0,08 (77 %)	31,5

Note: N – number of patients; \* – reliability in comparison with control group (p < 0.05); # – reliability in comparison with baseline values (p < 0,05) K – the ratio between the activities of termolabile alkaline phosphatase and tartrate resistant acid phosphatase.

– the osteogenesis marker, revealed the stimulating action of zinc picolinate on osteoregeneration, associated with the formation or repairing of bone.

The results show a statistically inconclusive increase of the activity of total alkaline phosphatase and termolabile alkaline phosphatase in the blood serum in the dynamic surveillance of patients who received standard treatment without zinc picolinate, which attests a weak osteoblast (odontoblast) reaction. However, total acid phosphatase activity and tartrate resistant acid phosphatase – osteodestruction marker, decreases insignificantly in all groups compared with baseline and control.

Practically, the acid phosphatase present in osteoclasts does not undergo changes in patients with periodontitis, while zinc picolinate has been shown to noticeably reduce enzyme activity by 31% ( $p < 0,05$ ) compared to the reference values of the control group. Compared to the control a statistical inconclusive reduction of enzyme activity is observed under the influence of standard medication. The obtained data indicates the stimulating effect on bone remodeling by suppressing the osteoclastic activity caused by zinc picolinate administration. At the same time, there is a reduction in the ratio of the activities of termolabile alkaline phosphatase and tartrate resistant acid phosphatase which, increases during the treatment with the zinc picolinate, revealing an increase in bone formation.

The results of the study of mineral metabolism indices are reflected in the statistics of Table 2.

The concentration of total calcium in blood serum in patients with periodontitis at the initial stage of research does not undergo significant changes compared with the control group. After the administration of zinc picolinate medication, calcium levels are maintained at the reference values. Standard treatment does not cause statistically reliable changes of the nominated index.

Also, there is initially a weak trend of reduction of the content of inorganic phosphate in the blood serum in patients with periodontitis. Medication with zinc picolinate produced some changes in the nominated index, thus the period of 6 months of the pathologic process is noted to increase the phosphate content by 12% ( $p > 0,5$ ) from baseline whereas standard treatment has not been shown to influence it.

The serum iron level in periodontitis decreases by 23-26% ( $p < 0,05$ ) compared with the control values. Standard treatment at all stages of research has shown a rising trend of iron content, but these changes are not statistically reliable. Medication with zinc picolinate prevents a decrease in the index in patients with periodontitis, which is demonstrated by the fact that at 6 and 12 months of the pathologic process the levels of serum iron in the specific group are maintained at amounts that exceeded the baseline and were statistically relevant.

The research carried out shows a statistically suggestive depression of zinc content in blood serum of patients with periodontitis comparing with the control group. The addition of zinc picolinate determined an increase in the content of zinc, which exceeded by 43% baseline values by 43% and control group level by 30% ( $p < 0,05$ ). Standard treatment induces the restoration of serum zinc levels to that determined in the control group.

### Conclusions

1. In general, chronic periodontitis disorders of bone remodeling processes are manifested by decreased activity of termolabile alkaline phosphatase and of the ratio between the activities of termolabile alkaline phosphatase activity and tartrate resistant acid phosphatase, while the activity of tartrate resistant acid phosphatase suffers no changes.
2. Zn picolinate possesses pronounced osteoregenerative properties which are manifested by stimulating bone

Table 2

The concentration of total calcium, inorganic phosphate, iron and zinc in blood serum in patients with periodontitis with the application of titanium implants and zinc picolinate administration

Research conditions	N	Total calcium (mmol/l)	Anorganic phosphate (mmol/l)	Iron (mmol/l)	Zinc (mmol/l)
Control	20	2,56±0,23 (100%)	1,71±0,12 (100%)	21,43±0,23 (100%)	18,50±0,16 (100%)
<b>Standard treatment</b>					
Baseline	12	2,53±0,37 (99%)	1,58±0,18 (92%)	16,54±0,26* (77%)	16,12±0,39* (87%)
6 months	10	2,55±0,17 (100%)	1,66±0,27 (97%)	19,67±0,28 (92%)	17,89±0,81 (97%)
12 months	6	2,52±0,25 (98%)	1,70±0,25 (99%)	21,13±0,31 (99%)	18,37±0,42 (99%)
<b>standard treatment + zinc picolinate</b>					
Baseline	15	2,51±0,26 (98%)	1,56±0,18 (91%)	15,81±0,36* (74%)	16,92±0,26* (91%)
6 months	13	2,64±0,17 (103%)	1,75±0,20 (102%)	22,54±0,38# (105%)	24,17±0,61*# (130%)
12 months	8	2,57±0,27 (100%)	1,72±0,26 (100%)	23,19±0,40# (108%)	23,41±0,27*# (127%)

Note: N - Number of patients; \* - reliability in comparison with control group ( $p < 0,05$ ); # - reliability in comparison with baseline values ( $p < 0,05$ ).

termolabile alkaline phosphatase activity and reduction of functional level of tartrate resistant acid phosphatase in periodontitis.

3. The study revealed insignificant disturbances of calcium phosphate metabolism in periodontitis, with contents of iron and zinc decreased only in advanced stages of periodontitis.

4. Zn picolinate has the ability to modulate the processes of bone remodeling and shows a favorable effect on mineral metabolism changes caused by periodontitis.

5. The research carried out, confirms the prospective use of zinc picolinate as an effective remedy for correction of metabolic disturbances caused by periodontitis.

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## Структурно-функциональные изменения сердечно-сосудистой системы у больных хронической обструктивной болезнью легких

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### Morpho-Functional Changes of the Cardio-Vascular System in Patients with Chronic Obstructive Pulmonary Disease

The morpho-functional changes of the cardio-vascular system were studied in 75 patients with chronic obstructive pulmonary disease. In Holter-monitoring ventricular extrasystoles (VES) were registered with almost the same frequency in all three stages of COPD. Grouped supraventricular extrasystoles (SVES) were found in 6.9% of the cases of COPD in stage 1, in 14% in stage 2, and in 33.3% in stage 3 COPD. Myocardial ischemia was diagnosed in 32 patients, 42.6% of the total number of the study group. In stage 1 painful ischemia was found in 17.2% and painless myocardial ischemia in 20.6%, in stage 2 – 14.2% and 32.1%, and in stage 3 – 14.2 and 32.1%, more often in younger persons.

Key words: chronic obstructive pulmonary disease, myocardial ischemia.

### Schimbările morfofuncționale ale sistemului cardiovascular la bolnavii cu bronhopneumopatie obstructivă cronică

Schimbările morfofuncționale ale sistemului cardiovascular au fost studiate la 75 de bolnavi cu bronhopneumopatie obstructivă cronică. Prin intermediul Holter-monitorizării, s-au înregistrat extrasistole ventriculare (ESV) practic cu aceeași frecvență în toate 3 stadii ale BPOC. Extrasistole supraventriculare (ESSV) în grup s-au depistat la 6,9% din cazuri cu I stadiu al BPOC, la 14% – cu al II stadiu, la 33,3% – cu al III stadiu al bolii. La 32 de pacienți s-a depistat ischemia miocardului, ceea ce constituie 42,6% din numărul de bolnavi investigați. Ischemia doloasă s-a depistat la 17,2%, asimptomatică – la 20,6% dintre bolnavii cu I stadiu, la 14,2% și 32,1% – cu al II stadiu, la 14,2% și 32,1% – cu al III stadiu al bolii respectiv, și mai des se înregistra la persoanele mai tinere.

Cuvinte-cheie: bronhopneumopatie obstructivă cronică, extrasistolii ventriculare și supraventriculare, ischemia miocardului.