

# Improving of reparative osteogenesis in patients diagnosed with chronic generalised periodontitis

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## Abstract

Pathological condition of periodontal structures presents a most complicated and wide spread problem in modern stomatology. According to data provided by WHO the periodontal disorders affect from 55 % up to 99% of population between the ages of 15 to 20 years and varies from 65% up to 98% in the age group from 35 to 44 years.

It has to be emphasized that there is none a single efficient treatment of generalized chronic periodontitis. Therefore, it is vital to improve the existent methods and find the new ones in diagnosis and management of periodontal disorders. The latter remains an actual subject of modern periodontology and surgical stomatology and exceeds a strategic doctrine on the whole.

The article demonstrates the results gained by surgical treatment of chronic generalized periodontitis, III degree of severity obtained by administration of bone-plastic material “Osteoplast-K” together with barrier membrane “Parodoncol” and pharmacological agent with immunomodulating effect «Extra Erbisol». We have observed the high efficiency of the recommended treatment that was proved by positive dynamic of alkali nephosphatase (ALP) in the blood serum of the main group over the period from 4 to 30 days by 21,7% comparing to the initial level ( $p < 0,05$ ). This investigation suggests that there is higher alveolar bone regeneration in the patients from the main group after the introduced treatment comparing to the control group. On the other hand, activity of aminotransferase did not changed significantly before and after operation in the control group. The findings also prove that there is no harmful influence of pharmacological agents used in this scheme.

## Keywords

chronic periodontitis, bone tissue, reparative osteogenesis, osteoplastic material

## Introduction

Periodontium is a complex and dynamic multi-tissue organization that comprises the root cementum, the periodontal ligament, marginal and attached gingiva and alveolar

bone. The periodontal tissues are connected genetically, morphologically and functionally. The findings provided by authors (Villar and Cochran 2010) demonstrated that the organization of alveolar bone and its physiological regeneration are very complicated. According to Offenba-

cher (1996) the maintenance of normal bone state requires balanced processes and conditions beginning with the genetic basis that provides pre- and postnatal histogenesis followed by diet, life style and oral hygiene.

The complex treatment of periodontal pathology presents one of the most actual problems nowadays. Chronic periodontitis can be considered as a risk factor for different systemic diseases. The prevalence of the disease, complicity and duration of the treatment introduce it as a central pathology not only in periodontology but also in general stomatology. Just as periodontal disorders are associated with multiple etiological factors, absence of donosological diagnosis and difficulties of early prophylaxis, they became extremely problematic to cure by conservative therapy.

Surgical method, on the other hand, is considered as a more radical approach in complex treatment of periodontal disorders. Aggressive periodontitis with resorption of alveolar bone caused by combined effect of microorganisms and disturbances of the tissues defense mechanisms is definitely indicated to surgical interference. The priority role is given to those protocols that can eliminate not only the source of inflammation, but also exclude pathological periodontal pockets, provide regeneration of the connective tissues including periodontal ligament (Nagirnyy 2011). All periodontal surgical interferences cause disorders in present cells and tissues associations and after the healing of the wounds (the inflammation) produce formation of a new anatomic-physiological links between the separated previously elements. This process consists of formation of the cloth, granulation tissue, epithelisation, production of collagen, regeneration and maturation. However, some classic surgical protocols in management of chronic periodontitis, have some disadvantages, for example, in protocol recommended by Melcher (1976) the quick apical epithelial proliferation that heal periodontal wound through formation of the long connective epithelium becomes an obstacle in regeneration of other tissues in an area of the defect. A nowadays approach of periodontal surgery is based on principles of guided tissue regeneration (GTR), that is a barrier formation for epithelial growth and by creating conditions for cluster growth of desmodontal and bone origin. It is important to preserve a certain volume for a required period of time by filling of the sub membrane space with young living tissues to sustain the shape and function of periodontium. By GTR this space is very individual; its geometry is defined not only by the roots, but also by a membrane. At the present phase the carriers from biodegradable materials are introduced into periodontal defects together with donor and bioactive components that are able to induce osteo- and angiogenesis. According to data researchers (Brodie et al. 2015) these implants should fill the defects and maintain the volume by their structure, conduce fast vascularization, have to be slowly resorbed by macrophages and osteoblasts, stimulate bone formation due to their unique composition of natural components- bone collagen, hydroxyapatite and sulfated glycosamino-glycans.

The administration of osteoplastic materials together with components of auto sourcing (plasma enriched with platelets, fibrin gel of auto blood, cultivated fibroblasts and autologous blood cells) is commonly used in maxilla-facial surgery and periodontology, enables significantly decrease the number of complications and reduce the timing of treatment. Fibrin gel of auto blood is considered as a perspective component of periodontal surgery. The polymerized fibrin gel develops a primary tissue matrix at the place of damage. According to Mazur (2012) the intact platelets interact with fibrin net and become activated. Low level in development of thrombin minimizes activation of platelets that slowly release growth factors, trigger this process that can last up to 7 days. Auto-thrombin gel prevents swelling and loss of fluids in the wound, stimulates angiogenesis and regeneration of epithelium, enhances synthesis of collagen, improves hemostatic effect, alleviates slow healing of the wound caused by glucocorticoids, increases concentration of leucocytes, creates a glue effect and integrates with other osteoplastic materials. The investigation suggests that administration of fibrin gel and bone plastic material "Osteoplast" has significantly decreased time of the treatment and the number of postoperative complications, therefore optimizing better healing and reparation.

The general therapy in case of operative treatment of periodontitis is multidirectional and includes wide range of pharmacological agents that are efficient immediately after the interference itself or improve reparative osteogenesis for a long period of time. The patients with chronic generalized periodontitis experience also immunological changes. The researches of (Vedyaeva et al. 2015) demonstrated that the decrease and misbalance of active T-cells and stimulation of B-cells suggest the need for immune correction as a part of the complex treatment.

It can be summarized that treatment of chronic generalized periodontitis of III degree by GTR-method together with osteotropic and immunomodulating agents confirmed pathogenetic based mode of their action and provides successful osteogenesis in the patients.

## Materials and methods

We have examined 76 people aged from 31 to 50 years diagnosed with chronic periodontitis of III degree. All examined patients were indicated for the flap surgery. Patients with other disorders, heavy tobacco smokers, those with bad oral hygiene and prosthesis of the affected areas and periodontitis of I-II degree were excluded from the research. The patients affected by chronic periodontitis and osteopenia were divided according to the treatment used on a main group with 40 people and a control group with 36 people randomly chosen by sex and age.

The study protocol was approved by the Ethics Committee of the Ivano-Frankivsk Naional Medical University (reference number: 50/10 registered 21.10.2010). Investigation was conducted in accordance with the Helsinki Declaration of 1975, as revised in 2008. According to the

requirements of bioethics all participants in study provided written informed consent for operation treatment and examination of biological materials.

Surgical methods in both groups were performed by a method of guided tissue regeneration (GTR). All members of the research diagnosed with chronic periodontitis were operated by flap surgery by Cishynskyy-Vidman-Neiman and administered with the mixture of Osteoplastic material "Osteoplast-K" and a fibrin gel from the patient's blood. The material "Osteoplast-K" („VITAPHORM-P" and OOO „LIKo-stom", Russian Federation, certificate of registration № 5098/2006, Order from 28.04.2006, Ministry of Health of Ukraine № 199, from 28.04.2006) is a not-demineralized bone collagen with minerals and sulfated glycosaminoglycans. This agent is sterile and appears as microchips, is also comparable with others bone-plastic materials and any organic and not organic substances without losing its qualities. There is a scheme for the preparation. The 10–20 ml of the vein blood should be collected (it depends on bone defect) and centrifuged 1–2 minutes after by the speed of 3000 rotation per minute. After 12 minutes there were 3 layers formed in the tubes: liquid, gel and red precipitate. After removal from the tube the fibrin gel was transferred into a sterile Petri dish.

The filled defects were covered by sterile collagen barrier membrane "Parodonnol" (ZAT «NPO «POLISTOM», Russian Federation, certificate of registration № 4774/2006, from 03.02.2006, Order Ministry of Health of Ukraine № 53, from 03.02.2006). The agent enhances osteogenesis and stimulates bone and periodontal healing and completely resorbs within 1, 5–2 months.

In the main group the immunostimulant "Extra Erbisol" (certificate of registration №UA/5036/01/01 approved by Ministry of Health of Ukraine 18.08.2006 №573) was used to adjoin surgical treatment. The agent was introduced intramuscular according to the instruction: every day twice a day by 2 ml (1 ampoule) in the morning and evening during 20 days (10 days before operation and 10 days after).

All patients were provided with general clinical examinations recommended by WHO for diagnosis of periodontal pathology.

The efficiency of recommended treatment has been assessed by estimation of ALP in blood serum that is considered as a marker of bone metabolism. Determination of activity of ALP was measured by spectrophotometric method. The obtained results of the serum enzyme's activity were compared with analogical data in healthy people: ALP<80

IU/L, Aspartate Aminotransferase (ASAT) from 11 IU/L to 40 IU/L, Alanine Aminotransferase (ALAT) – 5 – 40 IU/L).

Estimation of alkaline phosphatase in blood serum was performed before the research and then after 4, 16, 30 days and 6, 12 months since the beginning of the investigation.

The research lasted for 12 months.

## Results

The results obtained by laboratory investigations demonstrate that activity of ALP in control group before the research was (93,22±9,8) IU/L and exceeded the analogical data in healthy people by 16,5% and 28% in the main group with the data (102,46±9,2) (Table 1). There was no provable difference between the statistic among the control and main groups observed before the treatment ( $p > 0.05$ ).

The research indicates that ASAT remained within the norm in the patients from the control group before the treatment and excelled only by 10,7% in the main group comparing to the healthy people. Activity value of ALAT exceeded analogical numbers in healthy individuals by 7.7% and 18.2% accordingly. The indicators of ALAT in both main and control groups did not differ statistically before the treatment ( $p > 0.05$ ).

Activity of ALP in the control group has over numbered the initial data in 1.4–1.5 times ( $p < 0,05$ ) over the period of 4–16 days after the surgery. The ALP in this group has reached practically the same level as before the interference and was (96.77±7.7) IU/L by the end of 6 month. One year after the operation the index of ALP in the blood serum of the control group was (88.14±8.2) IU/L and slightly exceeded the norm.

The research demonstrates that there was an over rise of ALP by 57,5% in the blood serum of the patients from the main group over the postoperative period from 4 to 16 days in comparison with the healthy ones ( $p < 0,05$ ) and it kept high until the first postoperative month by 55% ( $p < 0,05$ ). As of 1 year after the interference the ALP has been within the norm.

Despite the fact that the average values of ASAT in the blood serum of the control group have increased by 15.4% and 7.9% accordingly over the period of 4–16 days after the operation, they were not statistically reliable ( $p > 0.05$ ). Already since 1 month after the interference the ASAT demonstrated the limits of generally accepted norm and the preoperative level. Analogical tendency is typical for the activity of ALAT: there was a rise ( $p < 0.05$ )

**Table 1.** Biochemical indicators of the blood serum before the treatment and dynamic of their changes influenced by recommended treatment in the patients affected by chronic generalized periodontitis.

Biochemical markers	Control group (n=40)						Main group (n=36)					
	Before treatment	4 days after treatment	16 days after treatment	30 days after treatment	6 months after treatment	1 year after treatment	Before treatment	4 days after treatment	16 days after treatment	30 days after treatment	6 months after treatment	1 year after treatment
ALP, IU/L	93,22±9,8	127,14±11,7*	141,11±12,0*	101,21±10,8	96,33±7,7	88,14±8,2	102,46±9,2	138,22±8,22**	129,17±7,88*	124,65±6,55	65,54±3,12****	67,22±3,67****
ASAT, IU/L	34,12±3,2	46,18±4,2*	43,18±2,9*	32,11±3,2	33,24±2,9	33,10±2,9	44,31±4,1	79,23±4,2****	86,12±5,0****	51,71±4,2***	35,38±2,4	40,24±1,9°
ALAT, IU/L	43,09±2,1	56,41±4,5**	48,92±3,4	32,41±2,8**	36,09±2,5*	33,89±2,3**	47,33±4,7	68,28±1,61***	62,9±2,4***	60,41±2,3***	54,05±2,01***	38,94±2,3

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

° – between the indicators of control and main group; ° – ( $p < 0,05$ ); °° – ( $p < 0,01$ ); °°° – ( $p < 0,001$ ).

at the 4<sup>th</sup> and 16<sup>th</sup> days ( $p < 0.05$ ) after operation by 41.0% and 22.3% accordingly and a further return of the level below preoperative ( $p > 0.05$ ) followed by normal indexes.

The indexes of ASAT dominated predominantly in patients from the main group after the administered treatment in the contrast with the patients from the control group over the period of 1 month by 37,4% ( $p < 0,05$ ). There were not any differences of ASAT between the groups over a year. However, ALAT in the patients from the main group at the postoperative period was statistically dominant upon the similar data of the 1 group from 11.4% ( $p < 0.05$ ) at the 4<sup>th</sup> day after surgery to 46.4% ( $p < 0.05$ ) in a month.

## Discussion

The ALP is present practically in all tissues of human body, but its high concentration is detected in osteoblasts and liver. Scientists argue that the ALP is considered as a marker of active osteogenesis and activity of osteoblasts. Therefore, the numeral changes of the distant molecular markers in case of periodontitis can be regarded as criterions of the efficiency in reparative regeneration of the bone tissues (Netyuchailo and Isheikina 2014a, b). The findings provided by authors (Melnychuk and Katerynyuk 2018) demonstrated that the decreased activity of ALP and increased amount of acid phosphatases a marker of the bone resorption in the blood and saliva of the patients are strongly depended on the severity of the disease.

ASAT and ALP are considered as cytoplasm enzymes that are released by the cells death or damage and an increase of enzyme activity is connected with the active periodontal inflammation. According to Gupta (2012) the severe gingival inflammation and loss of attachment are accomplished by a significant rise of ASAT in crevicular liquid.

The study findings suggest that an increased level of the serum enzymes such as ALP, ASAT and ALAT before the surgery indicate inflammation and destruction, but the gained results of the indexes do not prove the iraggressive

nature confirmed by clinical and radiological examinations (Kuznyak et al. 2015).

The level of ALP in postoperative period exceeded the norm in the control group patients by 26.5% and in the main group by 57,2% and has remained at high values up to 6 month. At the 12 month after the interference ALP was within the norm in the patients from both groups. The latter proves that the reparative process in the main group was more active comparing with the control group which is probably connected with introduction of Extra ERBISOL.

Analysis of the results demonstrates that activity of amino transphases during the postoperative period has not changed essentially in patients from the main group and they fluctuated within the norm. The difference in enzymes activity of the patients from both control and main groups is, in our opinion, influenced by active inflammatory processes, surgical interferences and administration of Extra ERBISOL. It allows to assert that materials used at the stages of operative treatment did not affect activity of amino transphases of the blood serum and thus did not have harmful influence on the organisms of the patients in general.

## Conclusions

In conclusion it can be summarized that the recommended treatment with administration of bone-plastic material "Osteoplast-K" together with a barrier membrane "Parodonkol" and an immunomodulating agent "Extra Erbisol" promote acceleration of periodontal regeneration proved by the results of biochemical investigations that is demonstrated in the increased activity of ALP by 21.7% up to 34.9% over the period from 4 to 30 days after the surgical interferences ( $p < 0.01$ ).

In addition, there is no evidence of biochemical changes in ASAT and ALAT at pre- and postoperative periods that indicates absence of any harmful influence of the introduced scheme on the patients affected by chronic generalized periodontitis.

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