# The Role of Prooxidant-Antioxidant System in the Development of Alveolitis after Teeth Extraction

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**Abstract**

The objective of research was to study the features of prooxidant-antioxidant status in patients with postoperative alveolitis. The study involved 2 groups – the control group (healthy) included 10 people; the main group (32 patients after tooth extraction in which postoperative alveolitis developed). To assess the intensity of lipid peroxidation processes in the oral cavity, the determination of the content of secondary products of lipoperoxidation by reaction with thiabarbituric acid was used. To evaluate the performance of the enzymatic link of the oral fluid actioxidant system (AOS), the enzyme activity of the first (superoxide dismutase (SOD) and second (catalase) lines of antiradical protection was determined. The level of malondialdehyde in patients with alveolitis was 1.9 times higher than in the control group; the level of hydroperoxide lipids also increased 8.1 times higher than the control group ($p < 0.05$). A study of the status of antioxidant protection in patients with postoperative alveolitis revealed a statistically significant decrease in SOD content by 51.0 % compared with the group of healthy individuals. Also, we observed a slight increase in catalase activity in the group of patients with alveolitis by 50.0 %.

The level of SH-groups in patients of the main group was 2.34 mmol / l and was by 58.6 % statistically significantly lower compared to the same indicator in the control group. Activation of free radical oxidation of biomolecules and depletion of both non-enzymatic (SH-group) and enzymatic (superoxide dismutase) levels of antioxidant protection are observed in the oral fluid of patients with alveolitis, as well as a compensatory increase in catalase activity.

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## Introduction

Tooth extraction surgery is one of the most common surgeries in dental practice. The number of complications is very large. They are general and local. The most common post-extraction complication is lumbar alveolitis. According to various authors, inflammation after tooth extraction occurs from 15 % to 35 %.[1,2] The literature provides sufficient evidence to demonstrate the effectiveness of sound oral hygiene to prevent the development of inflammatory complications after surgery to remove a tooth, that necessitates a comprehensive study of their mechanisms.

Recent studies have experimentally and clinically demonstrated the key role of lipid peroxidation (PLO) in the development of toxic hypoxia in a number of pathological conditions, in particular post-extraction alveolitis.[3,4,5] Currently, there has been a growing interest in the clinical aspects of the study of the processes of free radical lipid oxidation in dentistry. This is largely due to the fact that a defect in this metabolism is able to significantly reduce the resistance of the organism to the effects of adverse environmental factors, as well as to create the preconditions for the formation and acceleration of alveolitis.[6,7]

A high level of PLO is a general nonspecific

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reaction of the body to the influence of stress factors that stimulate the formation and accumulation of free radicals.[8] The effect of increased PLO is a membrane-toxic effect that leads to cell disintegration and depletion of the antioxidant protection system.[9] The role of oxidative stress, which is an imbalance between prooxidants and antioxidant defense mechanisms of the body, the main central pathogenesis of a number of acute and chronic conditions and diseases, in particular, postoperative alveolitis, is becoming increasingly clear as modern ideas develop. Since the mechanisms of antioxidant protection are universal for all cells, regardless of structural and tissue organization, it was expedient to study the features of prooxidant-antioxidant status in patients with postoperative alveolitis.

The objective of our research was to study the features of prooxidant-antioxidant status in patients with postoperative alveolitis.

## Materials and methods

Clinical observations and methods of laboratory and instrumental research were conducted at Ternopil State Medical University by I.Ya. Horbachevsky, Department of Surgical Dentistry. Special researches were carried out at the State Institution “Institute of Dentistry of the Academy of Medical Sciences of Ukraine”.

The study involved 2 groups – the control group (healthy) included 10 people; the main group (32 patients after tooth extraction in which postoperative alveolitis developed) received the following treatment: patients were washed a tooth hole with a solution of furacillin (1: 5000), leaving iodine turund in it. Patients independently did mouthwash with a warm hypertonic solution. All patients were prescribed analgesics and an antibiotic (ofloxacin).

All procedures performed in studies involving human participants were in accordance with the ethical standards of Bioethical Committee of Ternopil State Medical University and with the 1964 Helsinki declaration and its later amendments.

For biochemical research, non-stimulated oral fluid was collected from recipients according to conventional methods.[10] The resulting liquid oral centrifuged at 3000 rev / min for 15 minutes. For further study, both the supernatant and the precipitate were used.

To assess the intensity of lipid peroxidation processes in the oral cavity, the determination of the content of secondary products of lipoperoxidation by reaction with thiabarbituric acid was used. The principle of the method is based on the formation of a colored complex by the interaction of secondary products of lipoperoxidation (malondialdehyde (MA) and hydroperoxide lipids (HPL)) contained in the oral fluid. The color intensity of the formed complex, which was measured photometrically at a wavelength of 540 nm, is directly proportional to the concentration of the secondary products of the PLO. The results obtained were expressed in micromoles per 1 liter of oral fluid.[11,12]

To evaluate the performance of the enzymatic link of the oral fluid actioxidant system (AOS), the enzyme activity of the first (superoxide dismutase (SOD)) and second (catalase) lines of antiradical protection was determined. The activity of SOD was determined by the method of VA Kostyuk et al.[13]

The method is based on the ability of SOD to inhibit the reaction of quercitin auto-oxidation due to the dismutation of superoxide anion radical, which is formed by the oxidation of quercetin in the presence of N, N, $N_1$, $N_1$ - tetramethylethylenediamine under aerobic conditions. The specific activity of SOD was expressed in units of up to 1 g of protein of the oral fluid.

Catalase activity was determined by the colorimetric method.[14] The principle of the method is based on the ability of hydrogen peroxide to give a stable colored complex with molybdenum salts. Catalase activity was evaluated by the amount of hydrogen peroxide not destroyed by the enzyme. The enzyme activity was expressed in mkats/l.

The state of the non-enzymatic link of AOS oral fluid was judged by the level of non-protein thiol groups (SH-groups). The principle of the method based on the ability of low molecular weight thiol compounds in the interaction with 5, $5_1$-dinitro-bis- (2-nitrobenzoic) acid to form painted compounds - thio-2-nitrobenzoic acid, an aqueous solution of which has a maximum absorption at 412 nm. The results obtained were expressed in mmol/l oral fluid.[15]

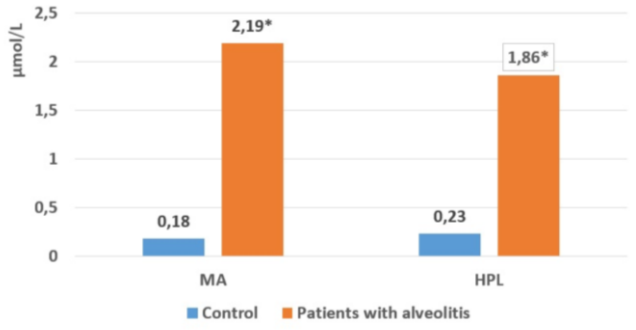
### Statistical analysis

Statistical processing of the received data was performed on a personal computer using standard software packages of Microsoft Excel

and with help of the computer program Statistica for Windows version 6.0 (Stat Soft inc., USA). The results were presented as mean values (M) ± the error of the mean (m). A level of p <0.05 was considered significant.

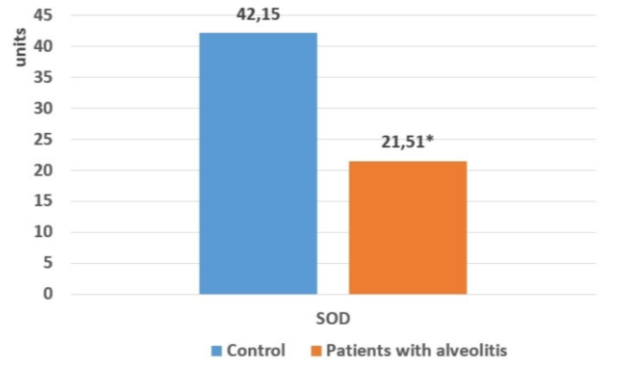
## Results

In the study of the status of PLO in patients with postoperative alveolitis revealed a significant activation of the processes of lipoperoxidation. In particular, the level of MA in patients in this group was 1.9 times higher than in the group of healthy individuals (p < 0.05). The level of HPL also increased 8.1 times higher than the control group (p < 0.05). Therefore, inflammation of the tooth hole after its extraction contributes to a significant activation of the processes of sex.




Note: * - the significant difference regarding to the same indicators in the control group (p <0.05).

**Figure 1.** Indicators of lipid peroxidation system in patients with alveolitis.

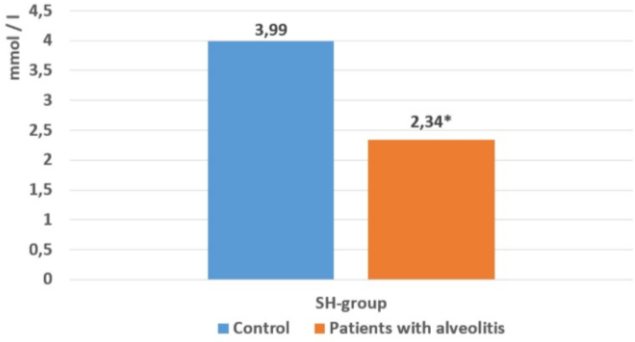



Note: * - the significant difference regarding to the same indicators in the control group (p <0.05).

**Figure 2.** Level of superoxide dismutase in patients with alveolitis.

A study of the status of antioxidant protection (AOP) in patients with postoperative alveolitis revealed a statistically significant decrease in SOD content by 51.0 % compared with the group of healthy individuals (p < 0.05). Regarding catalase activity in saliva, its content in patients with postextraction alveolitis was (5.27 ± 0.01) mkat/l, and in the healthy group it was (4.41 ± 0.16) mkat/l. Thus, we observed a slight increase in catalase activity in the group of patients with alveolitis by 50.0 %.

Investigation of the non-enzymatic system of AOP in patients with post-extraction alveolitis showed its significant suppression. The level of SH-groups in patients of the main group was 2.34 mmol/l and was by 58.6 % statistically significantly lower compared to the same indicator in the control group. In this group, the level of SH-groups was 3.99 mmol/l.




Note: * - the significant difference regarding to the same indicators in the control group (p <0.05).

**Figure 3.** Level of SH-group in patients with alveolitis.

Therefore, inflammation of the tooth hole after its extraction promotes the activation of the processes of peroxidation and inhibition of the mechanisms of AOP.

## Discussion

Oxidative stress and inflammation are closely linked. Inflammation is one of the manifestations of oxidative stress and simultaneously activates the generation of inflammatory mediators, such as adhesion of interleukin molecules, which in turn have been induced by oxidative stress. One of the most important consequences of the formation of reactive oxygen species is the enhanced and uncontrolled activation of the LPO processes, which may result from a sharp change in the oxygen regime of the cell.[16] Therefore, it is quite logical that we have obtained the results of studies in the oral cavity growth of the content of LPO products in patients with postoperative alveolitis. Thus, the content of the initial products

of LPO – HPL in the mouth fluid of patients, compared to the control group increased by 8.1 times, and the intermediate product – malondialdehyde – exceeded 1.9 times. Activation of free radical reactions with the accumulation of LPO products in the oral cavity of patients with alveolitis may contribute to the further progression of this pathology. LPO products are capable of damaging major connective tissue components, in particular collagen. Under the conditions of action of free radicals and products of free radical oxidation, the elasticity of collagen fibers is reduced, the processes of their renewal are disturbed, the processes of hydroxylation of amino acid residues in the collagen molecule are increased, which in turn increases the content of oxyproline and oxylysin.[17] This can significantly affect periodontal tissues and aggravate the course of the alveolitis.

There are conflicting and mixed data that explain the reasons for the sharp shift of the pro- / antioxidant equilibrium towards the prooxidant direction by spontaneous or spontaneous oxidation. According to the literature, one of the reasons for the violation of the prooxidant-antioxidant balance in the oral cavity in the alveolitis is the activity of antioxidant enzymes, which indicate the development and increase of functional failure of enzymatic and non-enzymatic units of AOS. It is known that the main mechanism of antioxidant protection in natural conditions is the enzyme SOD, whose high oxidation ability allows you to inactivate free radicals at the site of formation, preventing their diffusion.[18] Thus, the activity of the enzyme of the first line of antiradical protection – SOD in the oral fluid of patients with alveolitis was lower compared with the data in the control group. SOD activity decreased by 51.0 % compared to the control. According to the literature, there are three types of enzyme under study: Mn, Fe and Cu-Zn-containing SOD, the most fully studied is the structure of Cu-Zn-SOD, which is formed of two identical subunits, each of which has one atom of copper and zinc. Copper is involved in the catalytic function, and zinc plays a purely structural role.[19] The study of the effects of oxidative stress has shown that SOD is more important than catalase, to prevent oxygen-dependent inhibition of growth and induction of mutation. Some studies have shown that SOD, like catalase, is an inductive enzyme whose amount depends on external oxidative stress.

In the study of changes in the activity of the enzyme of the second line AOP – catalase, revealed opposite changes. In the clinical group of patients with alveolitis enzyme activity was higher by 50.0 % compared to the activity of catalase in people in the intact group. Such multidirectional changes between the activity of the enzymes of the first and second lines of antiradical protection indicate an imbalance in the work of the AOS enzymatic link. Inhibition of SOD in the oral fluid of patients with alveolitis creates conditions for the accumulation of reactive oxygen species in the oral cavity. In turn, an increase in the intensity of the free radical processes can cause inhibition of SOD activity due to irreversible reduction of copper in the active center or oxidation of functional groups, in particular thiols. With the growth of reactive oxygen species in the environment, conformational rearrangements of the enzyme molecule are likely to lead to the loss of their functional properties. The increase in catalase in the oral cavity of patients with alveolitis may be due to both increased synthesis of the enzyme and its recretion by salivary glands from the blood.[20]

Postoperative alveolitis has a significant effect on the condition of the non-enzymatic link of the AOS of the oral cavity. These patients had a 58.6 % decrease in non-protein SH-groups in the oral fluid compared with the concentration of non-protein SH-groups in the mouth of practically healthy people.

Depletion of AOP, accumulation of LPO products in the oral cavity can be caused by insufficient intake of antioxidant alveolitis by the patient. Due to the loss of teeth in patients is impaired chewing function, which is reflected in the course of digestion in the distal parts of the gastrointestinal tract, as well as the supply of nutrients to the blood and their subsequent use by the tissues of the human body.[21] Enhanced formation of initiators of free radical oxidation can deplete the pool of non-enzymatic antioxidants that, by fulfilling the role of free radical traps, are transformed into inactive metabolites. Deterioration of microcirculation of periodontal tissues observed with alveolitis and the attachment of microflora, reduces the supply of antioxidants, which increases the imbalance in AOS.

## Conclusions

In the oral fluid of patients with alveolitis activation of free radical oxidation of biomolecules and depletion of both non-enzymatic (SH-group) and enzymatic (superoxide dismutase) level of antioxidant protection, as well as the compensatory increase of catalase activity are observed.

## Declaration of Interest

The authors report no conflict of interest.

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