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# LIPID PEROXIDATION AND ANTIOXIDANT ACTIVITY IN ORAL FLUID OF PATIENTS WITH CHRONIC GENERALIZED PERIODONTITIS: EFFECT OF PERIODONTAL TREATMENT

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**Introduction.**

Chronic generalized periodontitis is an oral inflammatory disorder that gives rise to tissue damage and loss, as a result of the complex interaction between pathogenic bacteria and the host's immune response [1]. Evidence is accumulating which suggest that oxygen derived free radicals and their products play an important role in pathogenesis of chronic inflammatory disorder like periodontitis. Free radical may be defined as "any species capable of independent existence that contains one or more unpaired electrons." Prime targets of reactive oxygen species (ROS) are polyunsaturated fatty acids (PUFA) in membrane lipids causing lipid peroxidation. Malondialdehyde (MDA) is formed by peroxidation of PUFA and is used as a measure of lipid peroxidation [2]. The living organism has adapted itself to an existence under a continuous efflux of free radicals. Among the different adaptive mechanisms, the antioxidant defense mechanisms are of major importance. Antioxidants are "those substances which when present in lower concentration compared to that of an oxidisable substrate, will significantly delay or inhibit oxidation of that substance." The antioxidants like vitamin-E, vitamin-C, ceruloplasmin, quercetin, glutathione peroxidase and superoxide dismutase (SOD) protect tissue damage induced by free radicals [3, 4].

Efficiency of local application of medical drugs in periodontal tissues depends on the display of substances in the periodontal pocket (PP), choice of medical substances, method of his application, contact with oral mucosa and its concentration. Therefore it is necessary advantage to give to the forms and pathways of medications with the controlled and long action [5, 6]. Development and application high-efficiency and safe facilities of drug therapy of chronic generalized periodontitis (HGP) the last years legally considered one of priority directions of native and foreign researchers [7, 8, 9]. Medical local therapy is inalienable part of complex treatment of HGP [10].

Liposomes, owing to their small size, penetrate the regions that may be inaccessible to other delivery systems. It is noteworthy that only liposomes have been largely exploited for drug delivery because the methods of preparation are generally simple and easy to scale-up. The aim of using liposomal carriers is generally, to increase the specificity towards cells or tissues, to improve the bioavailability of drugs by increasing their diffusion through biological membranes, to protect them against enzyme inactivation. These systems reduce the frequency of administration, further provide a uniform distribution of the active agent over an extended period of time [11, 12].

Anti-inflammatory properties of «Lipoflavon» (JSC „Biolek", Kharkiv, Ukraine), which contained lecithin liposomes and quercetin are conditioned by his expressed anti-leukotrienes activity. Quercetin inhibits production of inflammation-producing enzyme 5-lipoxygenase.

**The aim of this study** to measure lipid peroxidation (MDA as an end product of oxidative stress) and corresponding antioxidant activity (SOD) in patients with HGP of initial-I degrees of severity and assess the influence of periodontal treatment with gel from the Granules of Quercetin (GQ) and Liposomal Quercetin-Lecithin Complex (LQLC) on these parameters.

**Material and Methods.**

The 35 patients with HGP of initial-I degrees of severity were observed. In accordance to treatment all patients were divided into 2 groups: I group - basic treatment with local application LQLC (18 patients) with using of individual periodontal delivery tray; II group (group of comparison) - basic treatment with local application of gel from GQ (17 patients) with using of individual periodontal delivery tray. The control group (C) included 14 healthy subjects without systemic inflammatory diseases.

The patients of basic group were conducted base therapy with the local application LQLC (injection form of «Lipoflavon») as a suspension, prepared extempore containing 137,5 mgs of Lecithin and 3,75 mgs of Quercetin. This suspension prepared at a premix 1/4 parts of content of small bottle with 5 ml 0.9% solution of natrium chloride, warmed-up to $38^0$. The patients of comparison group were conducted base therapy with local application of gel from GQ with using of individual periodontal delivery tray for 40 minutes 2 times per a day during 10 days.

All observed patients in the morning were conducted of oral fluid (OF) before treatment and through 1, 6 and 12 months after treatment for lipid peroxidation and antioxidant activity researches. Through 6 months the patients were examined, inspected the condition of periodontal tissues and conducted supporting therapy which included the professional hygiene of oral cavity and local treatment using of individual periodontal delivery tray with gel from GQ and LQLC during 10 days for 40 minutes 2

times per a day, and also reception inward during 1 month of 1 g «GQ» 2 times per a day.

**Results and discussion.**

The patients of control group were measured in OF: MDA - 4.62 ± 0.23 μmol/l and SOD - 4.73 ± 0.11 y.o. Imbalance between oxidative stress and antioxidant capacity may play a role in the pathogenesis of periodontal disease. Non-surgical periodontal treatment leads to a reduction of MDA and to levels comparable to healthy controls. ROS cause toxic effects by oxidative damage to macromolecules such as proteins, lipids and nucleic acids. The present study revealed extensive increase MDA in both groups of periodontitis which was a resultant of concomitant increase in ROS production. Thus, large amounts of pro-oxidants are produced in prolonged inflammatory response, as seen in periodontitis.

Antioxidants by counteracting the harmful effect of free radicals protect structural and tissue integrity. Imbalances between free radicals and antioxidants have been suggested to play an important role in the onset and development of several inflammatory oral diseases like periodontitis. Antioxidant enzymes like SOD provide protection against oxidative injury from oxygen free radicals. The function of SOD is to remove damaging ROS from the cellular environment by catalyzing the dismutation of superoxide radicals to $H_2O_2$. The total antioxidative potential of the plasma reflects the ability of an individual to resist the oxidative stress [13, 14].

The patients with initial-I degrees of severity in the basic group before treatment were measured in OF: MDA - 6.15 ± 0.61 μmol/l, that was higher than 33% in the C groups ($p$<0.05); SOD - 4.29 ± 0.18 y.o., that was lower than 9% in the C groups ($p$<0.05). The patients in the comparison group before treatment were meant MDA - 6.02 ± 0.58 μmol/l, that was upper than 30% in the C groups ($p$<0.05); SOD - 4.3 ± 0.19 y.o., that was lower than 9% in the C groups ($p$<0.05).

The patients with initial-I degrees of severity in the basic group after treatment through 1 month were measured in OF: MDA - 4.73 ± 0.57 μmol/l, that was higher than 2% in the C groups ($p$<0.05); SOD - 6.35 ± 0.18 y.o., that were significantly higher in periodontitis patients compared to controls upper than 48% ($p$<0.001). The patients in the comparison group after treatment through 1 month were measured in OF: MDA - 4.95 ± 0.51 μmol/l, that was higher than 7% in the C groups ($p$<0.001); SOD - 5.81 ± 0.21 y.o.; that was lower than 35 % in the C groups ($p$<0.001).

The patients with initial-I degrees of severity in the basic group after treatment through 6 month were measured in OF: MDA - 4.81 ± 0.25 μmol/l, that was higher than 4 % in the C groups ($p$<0.05); SOD - 5.51 ± 0.18 y.o., that was upper than 16 % in the C groups. The patients in the comparison group after treatment through 6 month were measured in OF: MDA - 4.86 ± 0.43 μmol/l, that was upper than 5% in the C groups; SOD - 5.27 ± 0.11 y.o., that was upper than 11 % in the C groups ($p$<0.003).

The patients with initial-I degrees of severity in the basic group after treatment through 12 month were measured in OF: MDA - 4.78 ± 0.33 μmol/l, that was higher than 3% in the C groups ($p$ < 0.05); SOD - 5.42 ± 0.13 y.o., that was upper than 15% in the C groups. The patients in the comparison group after treatment through 12 month were measured in OF: MDA - 4.91 ± 0.55 μmol/l, that was lower than 6% in the C groups; SOD - 5.02 ± 0.13 y.o., that was higher than 6% in the C groups ($p$<0.05).

**Conclusions.**

The research demonstrates pathogenetic role of abnormal processes of lipid peroxidation and antioxidant defense in the OF in their connection with clinical change in development of HGP of initial-I degrees of severity. The scheme of complex treatment of periodontitis by means of local application of lipoflavon using individual periodontal polyvinylchloride delivery tray contributing to inflammation elimination and long-term remission has been developed. High therapeutic efficiency of the LQLC was shown to be determined by antioxidant, membranotropic, anti-inflammatory effects. This allows to recommend lipoflavon for local application as pathogenetically substantiated drug in treatment of generalized periodontitis.

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**Резюме**

Результаты проведенных нами исследований показали патогенетическую взаимосвязь усиления процессов пероксидации липидов и снижения активности показателей антиоксидантной системы в ротовой жидкости с клиническими нарушениями в развитии генерализованного пародонтита хронического течения начальной-I степени тяжести. Высокий клинический эффект липофлавона обусловлен антиоксидантным, противовоспалительным и мембранопротекторным действием.

**Ключевые слова:** малоновый диальдегид, перекисное окисление липидов, супероксиддисмутаза, антиоксидантная активность, генерализованный пародонтит, патогенез, липофлавон.

**Резюме**

Результати проведених досліджень показали патогенетичний взаємозв'язок посилення процесів перекисного окиснення ліпідів та зниження активності показників антиоксидантної системи в ротовій рідини з клінічними розладами в розвитку генералізованого пародонтиту хронічного перебігу початкового-I ступеня важкості. Висока терапевтична ефективність ліпофлавона обумовлена антиоксидантною, мембранотропною, протизапальною діями.

**Ключові слова:** малоновий діальдегід, перекисне окиснення ліпідів, супероксиддисмутаза, антиоксидантна активність, генералізований пародонтит, патогенез, ліпофлавон.

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**Summary**

The research demonstrates pathogenetic role of abnormal processes of lipid peroxidation and antioxidant defense in the oral fluid in their connection with clinical change in development of chronic generalized periodontitis of initial-I degrees of severity. High therapeutic efficiency of the lipoflavon was shown to be determined by antioxidant, membranotropic, anti-inflammatory effects.

**Key words:** malondialdehyde, lipid peroxidation, superoxide dismutase, antioxidant activity, chronic generalized periodontitis, pathogenesis, lipoflavon.