DDC-UDC 616.314. – 17-008.18-002 DOI:10.19221/201818

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BIOCHEMICAL SUBSTANTIATION OF ADRENOBLOCKERS COMPLEX FOR TREATMENT OF PERIODONTAL DISEASES IN PATIENTS WITH PSYCHOSOMATIC STRESS

Abstract *In the development of periodontal diseases, the presence of psychological stress in patients is important. This should be taken into account in case of complex treatment of patients with periodontal diseases. To effectively treat periodontal diseases in these patients, it is necessary to experimentally substantiate the effectiveness of the proposed complex of adrenoblockers. Objective: experimentally substantiate the effectiveness of the proposed complex of adrenoblockers for the treatment of periodontal diseases. Methods: To substantiate the effectiveness of the proposed complex of adrenoblockers for the treatment of periodontal diseases, an experimental study was conducted on animals. Adrenaline stress was made in rats by oral application of gel with adrenalin in dose 0,36 mg/kg during 10 days. Lincomycin was introduced with drinking water in dose 60 mg/kg. T he gel of adrenoblocators (zocson + nicergolin and sibason) was introduced by application in dose 0,6 mg/kg. Conents of glucose, triglycerides, total cholesterine and malonic dialdehide (MDA), the activities of urease, lysozyme, elastase and catalase were determined into serum. Results: The conducted experimental studies have shown that the development of adrenalin stress causes in animals to increase the level of elastase, malonic dialdehyde. At the same time, the activity of catalase, antioxidant-prooxidative index decreases. The adrenoblocator gel reduced activity urease and content MDA, but raised activity catalase and antioxidant-prooxidative index. Conclusions. Oral application of gel with adrenoblocators made antidysbiotic action more then quertulyne, but yielded in antiinflammation and antioxidative actions to quertulyne after common introduce adrenaline and lincomycin. Thus, application of a gel with adrenoblockers produces an anti-inflammatory effect, but more definitely normalizes the processes of peroxidation of lipids.*
Keywords: *periodontal diseases, adrenaline stress, adrenoblocator, inflammation, antioxidant.*

Introduction. To date, periodontal disease is the most important problem in modern dentistry due to their significant distribution and treatment difficulties [4, 5, 12, 21, 22, 28].

In recent years, interest in neurogenic etiological factors, periodontal diseases, especially psychological stress has grown. It is shown that under the influence of chronic stress we see accelerated development of periodontal diseases, in particular generalized periodontitis [1, 23, 25, 26]. In particular, this is important among young people with a significant risk of periodontal disease [7, 20, 30]. It is shown that there is a certain correlation between the level of anxiety and periodontal diseases. All this requires the development of methods of medical correction of the stress situation in patients with periodontal disease.

In order to reduce the negative impact of psycho-emotional stress on the patient's body, a range of medicines for adrenoblockers was proposed: zoxone (0.002 g 1 time per day), nicergoline (0.005 g 3 times a day), sibazon (0.005 g once a day). This group of drugs is also used in other branches of medicine for the treatment of diseases such as arterial hypertension, etc. [2, 3, 11] and for the regulation of metabolic processes [10, 24].

The purpose of the experimental study was a comparative determination of the proposed complex of adrenoblockers on the periodontal tissue in conditions of reproduction in animals of the experimental periodontitis model.

Material and methods of research. For research, the following adrenoblockers were used: zoxon (dokazon modylate produced by the company Zentiva (Czech Republic), nicergoline ("Arterium" by the company "Galichpharm"

(Ukraine) and sibazon (diazepam) manufactured by "Interhim" (Ukraine), of which ex tempore prepared the gel, which was applied to the mucous membrane of the experimental animals.

The first series of experiments was carried out on 18 white rats of the Vistar line, which were divided into three groups. The first one - control, received the application of a gel without any medication. The second group received applications of gel blockers and the third received application of a gel with a control drug- atropine. Animals were withdrawn from the experiment after 30 days by bloodletting under thiopental anesthesia.

In the second series of experiments, the model of adrenalin stress [6, 9-11] was used. The development of a stressful situation is a characteristic change in the organism of animals and tissues of periodontal disease. In particular, the decrease in the activity of catalase and the content of total cholesterol, the activity of lysozyme, an increase in the degree of dysbiosis and the activity of the marker of inflammation elastase. The second series of experiments was performed on 21 white rats of the Vistar line (females, 13 months, live weight 290-330 g). Adrenalin stress was modeled daily by the use of gel containing adrenaline at a dose of 0.36 mg / kg of animal weight and the introduction of lincolicin in drinking water for 10 days. All animals were equally divided into three groups of 7 rats. The first group included animals that simulated only adrenaline stress. Animals of the 2nd (main) group on the background of adrenalin stress received daily gel treatment with proposed blockers (zoxon + nitrogolin + sibazon). The experiment lasted 10 days. Animals of the 3rd (control) group on the background of adrenalin stress received daily applications of a gel with a quartoline. The duration of all drugs in all groups was 10 days

. Euthanasia of rats was performed on the 11th day under thiopental anesthesia (20 mg / kg) by total bloodletting from the heart.

In serum, blood glucose [8], triglycerides [27], total cholesterol [27], malonic dialdehyde (MDA) [14, 19], urease activity [18], lysozyme [15, 16, 18], elastase [14, 19] and catalase [14, 19]. According to the ratio of relative activity of urease and lysozyme, the degree of dysbiosis according to Levitsky [15, 16, 18] was calculated, and according to the ratio of activity of catalase and the content of MDA, the antioxidant-prooxidant index of API [14, 19].

The activity of alkaline (LF) and acidic (KF) phosphatase [15-18], calcium content [15-18] and Lowry protein [15-18]) was determined in bone marrow homogenate. The mineralization index (MI) [15-18] was determined by the ratio of phosphatase activity (LF / KF), and the degree of mineralization (SM) was determined by the ratio of calcium and protein content [15-18]. The results were processed using standard statistical methods [13, 29].

Research results. Table 1 shows the results of determination in the gum level of markers of inflammation: elastase and MDA. From these data it is clear that adrenoblockers do not significantly affect the level of markers of inflammation, in contrast to atropine, which significantly increased the level of both markers: elastase by 35% and MDA by 25%.

Table 2 shows activity in the gums of urease and lysozyme. It is seen that blockers (and adrenoblockers, and atropine) do not significantly affect the activity of urease (atropine only shows a tendency to increase). At the same time, all blockers significantly increase the activity of lysozyme: adrenal blockers by 56%, and atropine by 111%. As a result of this oral applications and adrenoblockers, and atropine significantly reduce the degree of dysbiosis.

Table 3 presents the results of the determination of catalase activity and AII index in the gums. From these data it is seen that adrenoblockers significantly reduce the activity of catalase by 24%, whereas atropine practically

Table 1

Effect of adrenoblockers on the level of inflammation markers in the gums of rats (M±m)

№№ pp	Groups	Elastase, ukat/kg	MDA, mmol / kg
1	Control	32,5±3,9	22,6±1,2
2	Adrenoblockers	32,8±4,9 p>0,8	19,2±1,9 p>0,05
3	Atropine	43,9±3,5 p<0,05; p_1>0,05	28,2±2,0 p<0,05; p_1<0,015

Notes: p – compared to gr. 1; p_1 – compared with gr. 2.

Table 2

Effect of adrenoblockers on the activity of urease and lysozyme in the gums of rats (M±m)

№№ pp	Groups	Urease, ukat/kg	Lysozyme, unit / kg
1	Control	2,07±0,19	233±40
2	Adrenoblockers	1,97±0,12 p>0,3	364±49 p<0,05
3	Atropine	1,51±0,26 p>0,05; p_1>0,05	492±7 p<0,01; p_1<0,05

Notes: p – compared to gr. 1; p1 – compared with gr. 2

Table 3

Effect of adrenoblockers on the level of catalase and API index in the gums of rats (M±m)

№№ pp	Groups	Catalase, ukat/kg	API
1	Control	7,2±0,1	3,1±0,6
2	Adrenoblockers	5,5±0,4 p<0,01	2,9±0,2 p>0,6
3	Atropine	6,9±0,2 p>0,05; p_1<0,05	2,4±0,3 p>0,1; p_1>0,05

Notes: p – compared to gr. 1; p1 – compared with gr. 2

does not affect the activity of catalase. The API index does not change much after blockers.

In rats with adrenaline stress, an increase in glucose levels (to 7.46 ± 0.3 mmol / l), triglycerides (to 1.42 ± 0.1 mmol/l) and cholesterol (to 1.56 ± 0.08 mmol / l).

Application of gel with adrenoblockers in the rats of the main group causes a certain decrease in these parameters: glucose up to 7.63 ą 0.41 mmol / l, triglycerides up to 1.25 ą 0.37 mmol / l and cholesterol up to 1.85 ± 0.11 mmol / l In animals of the control group there was a similar decrease in these parameters: glucose to 7.15 ± 0.22 mmol / l, triglycerides - to 1.03 ± 0.09 mmol / l and cholesterol - to 1.90 ± 0.05 mmol / l . There was no statistically significant difference between the data of animals of the 2nd and 3rd groups (p> 0.05).

In rats with adrenaline stress, an increase in the marker of microbial contamination of urease (to 1.40 ± 0.14 nkat / l), a decrease in the level of protection - lysozyme (up to 63 ± 3 units / l) and an increase in the level of dysbiosis to 1.81 ± 0 , 22 units. Gel applications with blockers reduce the urease activity to 0.66 ± 0.21 nk / l and increase lysozyme levels to 73 ± 6 units / l. This leads to a significant reduction in the degree of dysbiosis - to 0.74 ± 0.20 units.

The development of adrenaline stress causes in animals changes in inflammation (elastase) and peroxidation (malonic dialdehyde - MDA) in animals. In particular, the level of elastase increases to 138 ± 10,4 ucat / l, and the content of MDA increases to 1.06 ± 0.06 mmol / l. Gel applications with adrenoblockers result in animals of the 2nd group to a significant decrease in these parameters: elastase to 112.4 ± 12.0 ucat/l and the MDA content to 0.90 ± 0.02 mmol / l.

Discussion. Studies have shown that adrenoblockers activate in gums lysozyme, reduce the degree of dysbiosis and the activity of catalase, increase the mineralization activity of periodontal bone tissue.

Thus, application of a gel with adrenoblockers produces an anti-inflammatory effect, but more definitely normalizes the processes of peroxidation of lipids.

Conclusions. The complex of adrenoblockers (zoxon + sibazon + nitsergolin) produces antidisbiotic, anti-inflammatory and parodontoprotective effects, as well as increases the level of the MI index.

References:

1. *Akhter R, Hannan M, Okhuba R, Morita M. Relationship between stress factor and periodontal disease in a rural area population in Japan. Eur. J. Med. Res. 2005; 10(8):352-7.*
2. *Bragin AV. Physiological appreciation of the patients with different stability of teeth to caries. Nauchnyi vestnik Tiumenskoi meditsinskoi akademii. 2001;(5):35-6.*
3. *Baraboi VA. The frey radical mechanisms of neurodegenerative pathology (review). Zhurnal AMN Ukraïni. 2001;7(2):219-31.*
4. *Chyzhevskyi IV. Klinichne ta hihiienichne obhruntuvannia profilaktyky kariiesu zubiv u ditei u promyslovo rozvynutomu rehioni [avtoref. dys.] Kyiv, 2010. 38 p.*
5. *Danilevskiy NF, Sidelnikova LF, Tkachenko AG. Rasprostranennost osnovnyih stomatologicheskih zabolevaniy i sostoyanie gigienyi polosti rta u naseleniya razlichnyih regionov Ukrainyi. Sovremennaya stomatologiya. 2006;2:14-6.*
6. *Den'ga OV, Makarenko OA, Tomilina TV.*

The methods of experimental pathology of periodontiume. In book: The Experimental stomatology. P. 1. The experimental models of Stomatological diseases (Levitsky AP, Shnaider SA.) Odessa: KP OGT; 2017. 68-102.

7. Deinzer R, Granrath N, Spahl M, Linz S, Waschul B, Herforth A. Stress, oral health behavior and clinical outcome. Br. J. Health Psychol. 2005;10(2):269-83.

8. Goryachkovskiy AM. Klinicheskaya biohimiya. Odessa: Ekologiya; 2005. 616 p.

9. Kononova OV. Vliyanie linkomitsina na sostoyanie parodonta u kryis s adrenalinovyim stressom. VIsnik stomatologii. 2016;96(3):26-8.

10. Kononova OV, Borisenko AV, Levitskiy AP. Vliyanie oralnyih geley kvertulina i adrenoblokatorov na sostoyanie parodonta u kryis s adrenalinovyim stressom. VIsnik stomatologii. 2016;97(4):8-11.

11. Kononova OV, Levitsky AP. The influence of lincomycin upon the biochemical indices in rat serum at stomatogenic action of adrenalin. Visnyk stomatologii. 2017;2(99):8-11.

12. Kosenko KM. Epidemiolohiia osnovnykh stomatolohichnykh zakhvoriuvan u naselennia Ukrainy i shliakhy yikh profilaktyky [avtoref. dys.] Kyiv, 1994. 45 p.

13. Lapach SN, Chubenko AV, Babich PN. Statistical methods in medical and biological research by using Excel. Kiev: Morion; 2000. 320.

14. Levitsky AP, Denga OV, Makarenko OA. Biochemical markers of inflammation of oral cavity tissue: method guidelines. Odessa: KP OGT; 2010. 16 p.

15. Levitskiy AP, Makarenko OA, Selivanskaya IA. Enzymatic methods for determination of oral dysbiosis for screening pro- and prebiotics: method guidelines. Kiev: GFC; 2007. 22 p.

16. Levitsky AP, Makarenko OA, Denga OV. The experimental methods of the study of osteogenesis stimulators. Kiev: GFK; 2005. 50 p.

17. Levitsky AP, Makarenko OA, Khodakov IV. The enzymatic method of the estimation of the state of osseous tissue. Odeskiy medychnyy zhurnal. 2006;3:17-21.

18. Levitskiy AP, Makarenko OA, Selivanskaya IA. Kvertulin. Vitamin R, prebiotik, gepatoprotektor. Odessa: KP OGT; 2012. 20 p.

19. Levitsky AP, Denga OV, Ivanov VS. The experimental dental caries. The experimental stomatology. The experimental models of stomatological diseases. Odessa: KP OGT; 2017. 59-67.

20. Omigbodun OO, Odukogbe AT, Omigbodun AO, Yusuf OB, Bella TT, Olayemi O. Stressors and physiological symptoms in students of medicine and allied health professions in Nigeria. Soc. Psychiatry Psychiatr. Epidemiol. 2006;41(5):415-21.

21. Ostapko OI. Naukove obgruntuvannia shliakhiv ta metodiv profilaktyky osnovnykh stomatolohichnykh zakhvoriuvan u ditei v rehionakh z riznym rivnem zabrudnennia dovkillia [avtoref. dys.]. Kyiv, 2011. 38 p.

22. Pavlenko OV, Antonenko MYu, Sidelnykov PV. Planuvannia likuvalno-profilaktychnoi dopomohy khvorym na heneralizovanyi parodontyt na osnovi otsinky ryzyku urazhennia parodontu. Sovremennaia stomatolohyia. 2009;1:56-61.

23. Pistorius A, Krahwinkel T, Willerhausen B, Bockstegen C. Relationship between stress factors and periodontal disease. Eur. J. Med. Res. 2002;7(9):393-8.

24. Ruenis AP, Rosalen PL, Volpato MC. Effects of caffeine and theophylline on the development of dental caries in rats. Biol. and Pharm. Bull. 2000;23(3):339-43.

25. Tarasenko LM. Patogenez povrezhdeniya parodonta pri stresse [avtoref. dis.] Moskva, 1986. 32 p.

26. Tarasenko LM, Petrushanko TA. Stress i parodont. Poltava: 1999. 192 p.

27. Tits NU. Entsiklopediya klinicheskih laboratornyih testov. Moskva: Labinfarm; 1997. 459-60.

28. Tkachenko AH. Osoblyvosti klinichnoho perebihu, likuvannia ta profilaktyky heneralizovanoho parodontytu u osib molodoho viku 18–25 rokiv [avtoref. dys.]. Kyiv, 2006. 20 p.

29. Truhacheva NV. Matematicheskaya statistika v mediko-biologicheskih issledovaniyah s primeneniem paketa Statistica. Moskva: GEOTAR-Media; 2012. 379 p.

30. *Smith CK, Peterson DF, Degenhardt BF, Johnson JC. Depression, anxiety, and perceived hassels among entering medical students. Psychol. Health. Med. 2007;12(1):31-9.*