pulse wave velocity and augmentation index@75 measured by oscillometric pulse wave analysis in Gujarati nonhypertensives. Vascular Investigation and Therapy.2018;2(1):50-55

16. Joyner M., Barnes J., Hart E, et al. Neural Control of the Circulation: How Sex and Age Differences Interactin Humans. Comprehensive Physiology. 2015;5(1):193-215. doi: 10.1002/cphy.c140005.

17. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Kidney Int. 2017; 7(1):1-59

18. Kim SY, Joo SJ, Shin MS, Kim C. Clinic and Home Blood Pressure Lowering Effect of an Angiotensin Receptor Blocker, Fimasartan, in Postmenopausal Women with Hypertension. Medicine (Baltimore). 2016; 95(22) - e3764. doi: 10.1097/MD.0000000000003764.

19. Kucukler N, Kurt IH, Topaloglu C, Gurbuz S, Yalcin F. The effect of valsartan on left ventricular myocardial functions in hypertensive patients with leftventricular hypertrophy. J Cardiovasc Med (Hagerstown).2012;13(3): 181-6. doi: 10.2459/JCM.0b013e3283511f00

20. Lang RM, Bierig M, Devereux RB, et al. Recommendations for chamber quantification: a report from the American Society of Echocardiography's Guidelines and Standards Committee and the Chamber Quantification Writing Group, developed in conjunction with the European Association of Echocardiography, a branch of the European Society of Cardiology. J. Am. Soc. Echocardiogr. 2005;18: 1440-1463.

21. Mackenzie IS, McEniery CM., Dhakam Z, et al. Comparison of the Effects of Antihypertensive Agents on Central Blood Pressure and Arterial Stiffness in Isolated Systolic Hypertension. Hypertension. 2009;54:409-413. DOI: 10.1161/HYPERTENSIONAHA.109.133801

22. Mancia G., Fagard R., Narkiewicz K. et al . 2013 ESH/ESC guidelines for the management of arterial hypertension.Hypertension. 2013;31:1281 – 1357 doi: 10.1097/01.hjh.0000431740.32696.cc

23. Nagueh S, Smiseth OA., Appleton CP, et al. Recommendations for the Evaluation of Left Ventricular Diastolic Function by Echocardiography: An Update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr.2016;29: 277–314.

24. Narayan O, Davies JE., Hughes AD. Central Aortic Reservoir-Wave Analysis Improves Prediction of Cardiovascular Events in Elderly Hypertensives. Hypertension.2015;65:629-635. DOI: 10.1161/ HYPERTENSIONAHA.114.04824.

25. Panagiota A, Areti T, Stella D. Hemodynamic and Arterial Stiffness Parameters in Ambulatory Blood Pressure Phenotypes and the Clinical Scenario of Polypharmacy and Comorbidities. The Journal of Clinical Hypertension 2015;17(8):655 doi.org/10.1111/jch.12544

26. Ruilope LM. Fixed-Combination Olmesartan/Amlodipine Was Superior to Perindopril + Amlodipine in Reducing Central Systolic Blood Pressure in Hypertensive Patients With Diabetes. J Clin Hypertens (Greenwich). 2016;18(6):528-35 doi: 10.1111/jch.12673.

27. Russo C, Jin Z, Palmieri V, et al. Arterial stiffness andwave reflection: sex differences and relationship with left ventricular diastolic function. Hypertension.2012;60:362–368 doi:10.1161/HYPERTENSIONAHA.112.191148

28. Salvetti M, Paini A, Bertacchini F, et al Changes in left ventricular geometry during antihypertensive treatment.Pharmacol Res. 2018;134:193-199. doi: 10.1016/j.phrs.2018.06.026.

29. Sohn SI, Kim CJ. Modulation of renin-angiotensin system and arterial stiffness: evidence from clinical trials. Curr Hypertens Rev.2014;.10(1):37-40. DOI : 10.2174/1573402110011411111603l1

30. Xiaoming Z, Cheng J, Yeqiang LD. Arterial Stiffness as a Predictor of Clinical Hypertension.The Journal of Clinical Hypertension. 2015;17(8): 582- 591 https://doi.org/10.1111/jch.12556

Maznichenko Iegor Aleksandrovich
postgraduate student, Odessa National Medical University

DYNAMICS OF IL-6 AND CK-18 CONCENTRATION IN BLOOD PLASMA IN PATIENTS WITH FAMILIAL HYPERCHOLESTERINEMIA WITH NON-ALCOHOLIC STEATOHEPATITIS AGAINST THE BACKGROUND OF STATIN THERAPY AND HEPATOPROTECTOR

Мазниченко Егор Александрович,
аспирант кафедры пропедевтики внутренних болезней и терапии,
Одесский национальный медицинский университет

Materials and methods. There was made a comprehensive examination of 71 patients with FHC and NASH and formed groups of patients: I - n = 35 with FHC and NASH receiving rosuvastatin 20 mg / day; II - n = 36 of FHC and NASH who received rosuvastatin and hepatoprotector "Hepadif" 2 capsules three times a day for 90 days. The results were evaluated on the 45th and 90th day of treatment.

Results. With rosuvastatin monotherapy, a decrease in the level of LDL (p = 0.001) and an increase in HDL (p = 0.01) were detected. Transaminase activity and IL-6, CK-18 concentrations tended to decrease but were not statistically reliable. In group II the LDL level reached the target value, transaminase activity was lower (p = 0.001). IL-6 concentration decreased significantly by 28% (p = 0.01), CK-18 - by 36.8% (p = 0.003).

Conclusions. Determination of IL-6 and CK-18 concentration has a strong positive relationship with hepatic transaminases and LDL level, so it is advisable to use IL-6 and CK-18 to select personalized therapy for patients with FHC and NASH.

Keywords: nonalcoholic steatohepatitis, familial hypercholesterolemia, hepatoprotector, interleukin-6, cytokeratin-18.

Introduction. Non-alcoholic fatty liver disease (NAFLD) is the most common chronic, diffuse liver disease, characterized by a slow course with a possible transformation into non-alcoholic steatohepatitis (NASH), liver fibrosis, cirrhosis, and hepatocellular carcinoma in severe cases [1,2,9,20].

It is now established that NAFLD is an independent predictor of cardiovascular diseases (CVD), an important risk factor of which is atherogenic dyslipidemia that is found in 20-80 % of patients with NAFLD [2,3,8,9,17,18]. Exacerbation of the pathological process with NAFLD leads to the transformation of steatosis into non-alcoholic steatohepatitis and is characterized by a deepening of the inflammatory response, impaired histoarchitectonics of hepatocytes, accompanied by hyperactive apoptosis of the latter [3,8,9,12,13,17,20]. It is proved that CVD pathogenetically determine the conditions for the development of hepatopathies [10, 17]. Patients with familial hypercholesterolemia (FHC) and NASH are an example of etiological comorbidity, which complicates the course of each disease and affects the long-term prognosis.

The golden standard of NASH diagnostics is a puncture biopsy, but the procedure has a significant range of disadvantages, which severely limits the use of the method, so the search for new non-invasive methods for liver pathology is continued [3,20]. A part of patients with steatosis or steatohepatitis are known to have referance values of hepatic transaminases activity, but inflammation and apoptosis continue in the liver tissue, resulting in loss of the liver parenchyma [1,9,20]. For the present, the informative determination of the level of the proinflammatory cytokine IL-6 in patients with NASH, which has a positive strong correlation with the level of hepatic transaminases and blood plasma cholesterol, has been proved [10,13].

Detection of the concentration of CK-18 in the blood plasma is now considered as a promising direction for the diagnosis of transformation of steatosis into steatohepatitis, as well as the determination of the stage of fibrosis (16), which may be an alternative to puncture biopsy, so timely diagnosis and pathogenetically justified therapy promotes good treatment [4,9,13].

The aim of this work was to increase the effectiveness of treatment of patients with familial hypercholesterolemia and non-alcoholic steatohepatitis, by conducting a comprehensive examination and determination of the concentration of IL-6, CK-18 in the blood plasma against the background of personalized hypolipidemic therapy in patients with FHC and NASH at the out- and in-patient stages.

Materials and methods. After a retrospective analysis of 218 case histories, 71 (n = 71) patients, 48±12 years of age, were included in the study, of whom 50 (46.3 %) were males and 58 (53.7 %) were females.

All patients underwent a comprehensive examination, which included taking of the anamnestic data, physical examination, laboratory (complete blood count, common urine analysis, biochemical studies of the blood serum: hepatic enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST) gama-glutamyltranspeptidase (GGTP), bilirubin and its fractions, thymol tests), lipidogram (total cholesterol (TC), low density lipoprotein (LDL), high density lipoprotein (HDL), triglyceride (TG), atherogenic index, fibrinogen, creatinine phosphokinase), immunological (thyrotropic hormone), fasting blood glucose, prothrombin index), enzyme immunoassay with determination of IL-6 concentration, CK-18 fragments in the blood plasma, instrumental examination (ultrasonography of the liver, elastography of the liver, ECG, echocardiographic examination of the heart).

The patients were divided into three groups by "simple randomization": the first group consisted of n = 35 patients (19 (54 %) women and 16 (43 %) men) having FHC with NASH that received standard lipid-lowering therapy, a SMC-CoA-reductase inhibitor - rosuvastatin “Rosucard” ("Zentiva", Czech Republic) internally, 20 mg / day; the second group consisted of n = 36 patients (20 (55.5%) women and 16 (44.5 %) men) having FHC with NASH who received similar statin therapy with additional administration of the complex hepatoprotector "Hepadif" ("Valartin Pharma", Ukraine/Kazakhstan). The control group consisted of 20 practically healthy individuals.

Verification of pathological conditions and somatic pathology was performed in accordance with the classification ICD -10. The diagnosis of FHC was made on the basis of the clinical guidance of the expert team of familial hypercholesterolemia of the US National Lipid Association "Family hypercholesterolemia: examination, diagnosis and treatment of adults and children" (2015). The diagnosis of NASH was made on the basis of the Order of the Ministry of Health of Ukraine No. 826 of 06.11.2014 and adapted clinical guidelines based on the evidence "Non-alcoholic fatty liver disease" (2014).

All examinations were performed according to the international standards for ethical research and biomaterials takingю

For the purpose of dynamic clinical and laboratory-instrumental monitoring, the patients were offered a schedule of visits on the 45th and 90th days of therapy.

The results obtained were processed using Microsoft Excel (Microsoft corporation, 2018) licensed software and SPSS Statistics 13.0 software package. The difference between the study indices in $p < 0.05$ was considered significant.

Results and Discussion. The analysis of the clinical examination data revealed complaints of the hepatobiliary tract in all patients. The patients of the first group complained of periodic nagging pain in the right hypochondrium n = 8 (23 %), sensation of heaviness and discomfort in the right hypochondrium was registered in 32 (91.4 %) patients, loss of appetite in 30 (88 %), general weakness in 32 (83 %) patients. In the second group of patients: pain in the right hypochondrium was noted by 5 (14 %) patients, heaviness and discomfort in the right hypochondrium by 34 patients (97.1 %), rapid fatigue was reported in 33 (91.6 %) patients.

According to ultrasonography and liver elastography in the first group patients liver steatosis of the stage 2 was detected in 21 (60 %) patients, steatosis was of diffuse character in 33 (94.3 %) patients, attenuation of the sound level of the diaphragmatic edge of the liver had 31 (88.6 %) of patients and according to elastography the liver density was up to 5.8 kPa in 28 (80 %) patients. In the second group of patients, steatosis of the stage 2 was detected in 22 (61 %) patients, the majority of patients – 33 (91.7 %) had a diffuse infiltration, the sound level attenuation was detected in 32 (89 %) patients, and according to elastography the liver density was up to 5.8 kPa in 27 (75 %) patients.

During the analysis of the first examination of the biochemical and immunological indices of the blood serum of patients of all groups there was revealed pronounced hypercholesterolemia, increased activity of hepatic transaminases and levels of IL-6, CK-18 in comparison with the control group ($p < 0.01$) (Table 1). The level of TC was 2 times higher than in the control group ($p < 0.01$), the activity of liver enzymes, in particular ALT and AST was three times higher than in the control group ($p < 0.01$), but the activity of GGTP in all investigated groups was at the level of reference values (Table 1).

Table 1

BIOCHEMICAL AND IMMUNOLOGICAL INDICES OF THE BLOOD SERUM OF PATIENTS WITH FHC AND NASH AT THE FIRST EXAMINATION

Index	Control group n=20	I group n=35	II group n=36
TC, mmol/l	4,24 ± 0,07	8,61 ± 0,52 *	8,63 ± 0,76 *
VLDL, mmol/l	0,33 ± 0,14	0,7 ± 0,11 *	0,69 ± 0,15 *
LDL, mmol/l	2,83 ± 0,13	5,21 ± 0,2 *	5,39 ± 0,32 *
HDL, mmol/l	1,24 ± 0,09	1,23 ± 0,12 *	1,21 ± 0,16 *
TG, mmol/l	1,05 ± 0,07	1,46 ± 0,16 *	1,16 ± 0,23 *
AC	2,4 ± 0,11	6,05 ± 0,14 *	6,11 ± 0,54 *
ALT, U/l	24,2 ± 2,3	107,5 ± 7,6 *	103,46 ± 5,2 *
AST, U/l	27,05 ± 1,82	97,5 ± 8 *	98,76 ± 3,43 *
GGTp, U/l	48,36 ± 2,4	47,4 ± 3,8	41,05 ± 5,68
IL-6	1,22 ± 0,22	5,0 ± 0,25 *	4,98 ± 0,22 *
CK-18	40,8 ± 7,3	371 ± 14 *	370,4 ± 12,2 *

Note: * - $p < 0.01$ relative to the control group.

On the 45th day of therapy, there was a tendency to decreasing the levels of lipidograms and the activity of liver enzymes indices, but they did not acquire statistical significance.

On the 90th day of hypolipidemic therapy with rosuvastatin the patients of the first group had a slight decrease in the severity of complaints of the hepatobiliary system: 6 (17.1 %) patients complained of periodic nagging pain in the right hypochondrium, heaviness and discomfort had 28 (80 %) patients. On physical examination, 7 (20 %) patients were revealed a distended abdomen and 30 (86 %) patients had liver enlargement. According to ultrasonography data liver steatosis of the stage 2 had 18 (51.3 %) patients; the sound level attenuation had 30 (85.8 %) patients.

A comparative analysis of the biochemical indices of the first group on the 90th day revealed a significant decrease in LDL by 27.1 % ($p = 0.001$) compared to the initial treatment, but the level of LDL did not reach the target indices and was higher by 31 % compared to the control group. The HDL level on the 90th day of treatment was significantly higher by 44.7 % ($p = 0.001$) compared to the baseline, and the TG level was lower by 17.1 %. The activity of the liver enzymes, in

particular ALT was lower by 17.4 %, AST by 14.3 % when compared with the initial data, but the statistical reliability was not reached. The activity of GGTP was at the level of baseline indices. The concentration of IL-6 on the 90th day was lower by 13 %, and the level of CK-18 - by 9.4%, but the statistical significance was not obtained (Table 2).

Table 2

BIOCHEMICAL AND IMMUNOLOGICAL INDICES OF GROUP I AND II PATIENTS ON THE 90TH DAY OF HYPOLIPIDEMIC THERAPY

Index	Control group n=20	I group n=35	II group n=36
TC, mmol/l	4,24 ± 0,07	7,97 ± 0,65 *	5,81 ± 0,74 *#
VLDL, mmol/l	0,33 ± 0,14	0,91 ± 0,11 *	0,47 ± 0,1 * #
LDL, mmol/l	2,83 ± 0,13	4,1 ± 0,23 *	2,53 ± 0,22 * #
HDL, mmol/l	1,24 ± 0,09	1,78 ± 0,11 *	2,14 ± 0,14 *#
TG, mmol/l	1,05 ± 0,07	1,71 ± 0,21 *	0,82 ± 0,11 *#
AC	2,4 ± 0,11	3,48 ± 0,14 *	1,73 ± 0,24 *#
ALT, U/l	24,2 ± 2,3	91,5 ± 10,8 *	44,5 ± 12,4 *#
AST, U/l	27,05 ± 1,82	85,3 ± 4 *	32,3 ± 4,38 *#
GGTp, U/l	48,36 ± 2,4	41,4 ± 4,7	47 ± 7,28
IL-6	1,22 ± 0,22 *	4,42± 0,36 *	2,92 ± 0,2 *#
CK-18	40,8 ± 7,3 *	339 ± 25 *	266,5 ± 19 *#

Note: * - p <0.05 relative to the control group; # - relative to the group I.

The patients of the second group who were additionally prescribed hepatoprotector against the background of statin therapy on the 90th day of therapy, were found to have a more significant reduction in the frequency of complaints: the patients did not complain of periodic, nagging pain, 4 patients (11.1%) had a feeling of heaviness and discomfort in the right hypochondrium, total weakness – 7 (19.4 %) patients. Physical examination showed liver enlargement in 20 (55.6 %) patients, abdominal distension in 4 (11.1 %) patients. Ultrasound examination revealed steatosis in big majority of 1 degree in (55.6 %), the liver density according to elastography was less than 5.8 kPa in 30 (86.1 %) patients.

When conducting a comparative analysis of the data obtained from the biochemical study of the blood serum of the patients in the second group there was revealed a significant decrease in the level of LDL (p = 0.001) compared to the baseline data, by 62 % less than in the first group (p = 0.02). The HDL level was significantly higher by 77 % (p = 0.001) compared to the baseline, by 20.2 % (p = 0.047) when compared to the first group. The activity of hepatic transaminases tended to decrease, so ALT, AST were significantly less (p = 0.001) almost one and a half times including less than the activity of the first group by 94.6 % (p = 0.01). The analysis of these immunological indices revealed a significant decrease of IL-6 by 70.5 % (p = 0.001), and the concentration of CK-18 was lower by 39 % (p = 0.001).

Thus, the use of rosuvastatin monotherapy reliably led to a reduction in LDL levels and an increase in HDL levels, but no target LDL levels were achieved. Regarding the activity of the liver enzymes, there was a tendency for a decrease in the activity and manifestation of the cytolytic syndrome as well as a decrease in the concentration of IL-6 and CK-18, but the indices did not reach reliable significance.

The use of rosuvastatin and complex hepatoprotector resulted in a more pronounced hypolipidemic effect, which was probably due to the action of hepatoprotector components that affected the metabolism of lipids in hepatocytes, had a protective effect on fatty dystrophy of the cells; indirectly affected the reduction of the cholesterol level in the peripheral blood [12,14,16,18]. Complex therapy contributed to a significant decrease in the level of LDL, an increase in the level of HDL; in addition, the target levels of LDL were achieved. A comparative analysis of the liver enzyme activity revealed a significant decrease in ALT and AST activity (p = 0.001) compared to the baseline and significantly lower activity compared to the first group, which had a positive correlation with a decrease in IL-6 concentration (r = 0.52) and CK-18 in the blood plasma (r = 0.53).

It is now established that in patients with steatosis or steatohepatitis the activity of the hepatic enzymes often does not exceed the reference values, but the disease is characterized by minimal inflammation due to apoptosis, during which the utilization of excessive number of apoptotic bodies increases the damage of the liver tissue and contributes to fibrosis formation [4,9,13]. It is believed that inflammation processes are a major factor in the transformation of steatosis into steatohepatitis [8,11,19]. NASH is a diagnosis of "exclusion", so to identify this pathology a comprehensive examination of patients is made [3,20]. Currently, there is no single standard of treatment for patients with NASH, including comorbid pathology, so the determination of IL-6 and CK-18 additional to standard laboratory tests is pathogenetically grounded, non-invasive diagnostic method that can be used to identify the stage of the disease and assessment of the treatment efficacy for the selection of personalized therapy of the patients and improvement of prognosis, disease course and quality of life of the patients with FHC.

Conclusions: 1. Hypolipidemic therapy with rosuvastatin in patients with FHC and NASH resulted in a significant decrease in the level of LDL ($p = 0.001$) and an increase in the level of HDL ($p = 0.001$), but the target levels were not reached. The activity of the liver enzymes had a slight downward tendency and coincided with a decrease in IL-6 by 13 %, and a decrease in CK-18 by 9.4 %, but no statistical reliability was obtained.

2. Complex hypolipidemic therapy with rosuvastatin and hepatoprotector led to a reliable decrease in the level of LDL and an increase in the level of HDL ($p = 0.001$), reaching the target levels of LDL. The activity of the liver enzymes was significantly lower compared to the baseline and the first group data ($p = 0.01$). IL-6 and CK-18 concentrations were reliably lower than the baseline and had a strong, positive correlation with indices of the liver enzyme activity ($r = 0.51$ for IL-6, $r = 0.53$ for CK-18).

3. In addition to the standard laboratory tests, the determination of proinflammatory IL-6 and CK-18 fragments should be used to evaluate the morpho-functional status of the liver and to select further tactics for the treatment of patients with FHC and NASH.

Further studies should be directed at the study of indices of proinflammatory cytokines and CK-18 fragments to determine the effectiveness of long-term complex hypolipidemic therapy, to evaluate the duration of effects after therapy, and to investigate the remote results of lipolipidemic treatment of familial hypercholesterolemia.

References:

1. Уніфікований клінічний протокол «Неалкогольний стеатогепатит». Наказ МОЗ України № 826 від 06.11.2014 року / М. К. Хобзей, Н. В. Харченко, О. М. Ліщина [та ін.] // 2014. [інтернет]. Доступно: http://mtd.dec.gov.ua/images/dodatki/2014_826Gepatyty/2014_826_YKPMD_NSTPT.pdf.

2. Маевская МВ, Моморзова МА. Возможности коррекции дислипидемии у пациентов с неалкогольной жировой болезнью печени. Гепатол. 2016;26(4):55-61.

3. Стаценко МЕ, Туркина СВ, Косивцова МА, Тыщенко ИА. Неалкогольная жировая болезнь печени, как мультисистемное заболевание. Вестник ВолгГМУ. 2016;2(58):8-14.

4. Bratoevka K, Nikolova S, Merdzhanova A, Stoyanov GS, Dimitrova E, Kashlov et al. Association between serum CK-18 levels and the degree of liver damage in fructose-inducted metabolic syndrome. Metab. Syndr. Relat Disord. Sep. 2018;16(7):350-7.

5. Clinical management of heterozygous familial hypercholesterolemia in a Polish outpatient metabolic clinic: a retrospective observational study / L. Klosiewicz-Latoszek, B. Cybulska, J. Bialobreska-Paluszkiewicz et all // Arch. Med. Sci. 2018;14(5):962 - 970.

6. 2016 ESC/EAS Guidelines for the management of dyslipidemias / Developed with the special contribution of the European Assocciation for Cardiovascular Prevention & Rehabilitation (EACPR) // Russ. J. Cardiol. 2017;5(145):P. 7 - 77.

7. Gidding SS, Champagne MA, Ferranti SD, Defesche J, Matthew K, Ito MK et al The agenda for Familial Hypercholesterolemia: a scientific statement from the American Heart Association. Circulation . Dec. 2015;132(22):2167 - 92p. doi:10.1161/CIR.000000000000029.

8. Hirsova P, Ibrahim SH, Gores GJ, Malhi M. Lipotoxic lethal and sublethal stress signaling in hepatocytes: relevance to NASH pathogenesis. J. Lipid Res. 2016. Oct;57(10):1758-70 p. doi: 10.1194/jlr.R066357.

9. Kanda T, Matsuoka S, Yamazaki M, Shibata T, Nirei K, Takahashi H et al. Apoptosis and non-alcoholic fatty liver diseases.World J. Gastroenterol. 2018. Jul;24(25):2661-72 p. doi: 10.3748/wig.v24.i25.2661.

10. Kim EJ, Kim BH, Seo HS, Lee YJ, Kim HH, Son HH at al. Cholesterol-induced non-alcoholic fatty liver disease and atherosclerosis aggravated by systemic inflammation. PloS One. Jun. 2014;9(6):e97841. doi: 10.1371/journal.pone.0097841. eCollection 2014.

11. Knottnerus FJG, Bleeker JC, Wust RCI, Ferdinandusse S, IJist L, Wijburg FA et al. Disorders of mitochondrial long-chain fatty acid oxidation and the carnitine shuttle. Rev endocor Metab Diord.Mar 2018;19(1):93-106p. doi: 10.1007/s11154-018-9448-1.

12. Liang X, He Q, Zhao Q. Effect of statins on LDL Reduction and liver safety: a systematic review and meta-analysis. Biomed.Res Int.Mar 2018;5:7092414 doi:10.1155/2018/7092414

13. Mandelia C, Collyer E, Mansoor S, Lopez S, Lappe S, Nobili V et al. Plasma cytoceratin-18 level as a novel biomarker for liver fibrosis in children with nonalcoholic fatty liver disease. J Pediatr Nutr. Aug. 2016;63(12):181-7p. doi: 10.1097/MPG.0000000000001136.

14. Naseem S, Hussain T, Manzoor S. Interleukin-6: a promising cytokine to support liver

regeneration and adaptive immunity in liver pathologies. Cytokine Growth factor Rev. Feb. 2018;39:36-45p. doi: 19.1016/j.cytogfr.2018.01.002

15. Sulivan EM, Pennington ER, Green WD, Beck MA, Brown DA, Shaikh SR. Mechanisms by which dietary fatty acids regulate mitochondrial structure-function in health and disease. Adv.Nutr. May. 2018;9(3):247-62p. doi: 10.1093/advances/nmy007

16. Schmidt-Arras D, Rose-John S. IL-6 pathway in the liver: from physiopathology to therapy. J Hepatol. June.2016:64(6):1403-15p. doi:10.1016/j.hep.2016/02.004

17. Tajiri K, Futsukaichi Y, Kobayashi S, Yasumura S, Takahara T, Minemura M et al. L-carnitine for the treatment of over hepatic encephalopathy in patients with advanced liver cirrhosis.J.Nutr. Sci. Vitaminol. 2018;64(5):321-28p. doi: 10.3177/jnsv.64.321.

18. Thota RN, Ferguson JJA, Abbott KA, Dias CB, Garg ML. Science behind the cardio-metabolic benefits of omega-3 polyunsaturated fatty acids: biochemical effects vs. clinical outcomes.Food Funct.Jul. 2018;9(7):3576-96p. doi: 10.1039/c8fo00348c.

19. Wang HH, Garruti G, Liu M, Porthincasa D, Wang DQ. Cholesterol and lipoprotein metabolism and atherosclerosis: recent advances in reverse cholesterol transport. Ann Hepatol. Nov. 2017:16(Suppl. 1: s3-105.); s27-s.42p. doi:10.5604/01.3001.0010.5495.

20. WGO Global Guidelines NAFLD/NASH, (2012), 32 P.

Mazur I. P., *Doctor of medicine*
Khlyebas S. V.,
Bakshutova N. O.
Shupyk National Medical Academy of Postgraduate Education

CLINICAL EFFICACY OF THE TREATMENT OF CHRONIC GRANULOMATOUS PERIODONTITIS USING A DRUG COMPOSITION BASED ON 2% CHLORHEXIDINE

Мазур І. П., *д. мед. н.*
Хлєбас С. В., Бакшутова Н. О.
Національна медична академія післядипломної освіти імені П. Л. Шупика

КЛІНІЧНА ЕФЕКТИВНІСТЬ ЛІКУВАННЯ ХРОНІЧНОГО ГРАНУЛЕМАТОЗНОГО ПЕРІОДОНТИТУ ІЗ ЗАСТОСУВАННЯ МЕДИКАМЕНТОЗНОЇ КОМПОЗИЦІЇ НА ОСНОВІ 2% ХЛОРГЕКСИДИНУ.

Abstract . Background. In Ukraine, according to the results of a statistical analysis of dental care, the proportion of treated teeth with complicated caries in relation to all treated teeth in healthcare facilities of all forms of ownership is increasing, and the number of complaints about chronic periodontitis is increasing. The insufficiently high efficiency of treatment of infectious and inflammatory processes in the periapical tissues, an increase in the frequency of destructive forms of periodontitis necessitates the search for new and effective treatment methods.

Objective. To study the effectiveness of the use of the developed drug composition based on 2 % chlorhexidine during endodontic treatment in patients with chronic granulomatous periodontitis.

Materials and Methods. A clinical and radiological study of the effectiveness of treatment of 32 patients with chronic granulomatous periodontitis was carried out. Patients of the main study group included a drug composition in the treatment protocol that contains 2 % chlorhexidine (administered for 3 days) under an airtight light-curing bandage. Patients in the control group were treated with calcium hydroxide (administered for 7 days) under an air-tight light-curing bandage. The effectiveness of treatment was evaluated on the basis of clinical and radiological data before treatment, after treatment, after 6 and 12 months.

Results. According to the results of a comparative clinical and radiological study, it was proved that the use of a drug composition based on 2% chlorhexidine in patients with chronic granulomatous periodontitis is highly effective ($p < 0.001$). According to the results of X-ray observation, a reduction in the focus of the infectious and inflammatory process in the periapical tissues, a decrease in the destruction area in the periapical area after 12 months in the main group by 97.3 % (from 3.31±0.10 mm2 0.09 ± 0.06 mm2) ($p<0.001$) in comparison with the control group (area reduction by 88.8%: from 3.34±0.11 mm2 to 0.64±0.024 mm2) ($p<0.001$). Complications or allergic reactions during treatment and during the observation period, cases of exacerbation of the process or relapse of the disease were not registered, which indicates the safety of the drug composition based on 2 % chlorhexidine.

Conclusion. Based on the obtained clinical and radiological research results, it is possible to confirm the effectiveness and feasibility of using a drug composition based on 2 % chlorhexidine in the treatment of patients with chronic granulomatous periodontitis. The high clinical effectiveness of the proposed method of treatment is due to the prolonged antibacterial effect of chlorhexidine on the root canal system, a decrease in inflammatory processes in the periapical tissues, which positively contributes to the process of reparative regeneration of bone tissue in the area of the apex of the root of the tooth, and also increases the efficiency and reduces the time of endodontic treatment, while reducing financial expenses.