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#### IMPACT OF THERAPY UPON CYTOKINE PROFILE AMONG PATIENTS WITH HYPERTENSIVE TYPE OF CHRONIC GLOMERULONEPHRITIS

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**The objective of this work** is to carry out a comparative estimation of an impact of anti-hypertension therapy upon the contents of anti-inflammatory cytokines (factor of tumour necrosis –  $\alpha$  – FTN- $\alpha$ , interleukin-1b, IL-1b, IL-6, soluble receptor of IL-6) in blood serum of patients with hypertensive type of chronic glomerulonephritis (CGN).

**Methods and materials.** 96 patients with hypertensive type of CGN with disease period of 1 to 10 years without disturbance of kidney function (GFR > 60 ml/min) have been under observation. The average age of patients equaled  $44,3 \pm 5,8$  years. Diagnosis CGN was established according to anamnesis and clinical-laboratory research. On average, daily proteinuria did not exceed  $0,5 \pm 0,2$  g/day among the studied patients. Average speed of glomerular filtering equaled  $83,5 \pm 2,2$  ml/min. Arterial hypertension (AH) among patients with CGN was defined according to recommendations of Russian scientific society of cardiologists (2010). Control group was formed of 30 healthy donors aged from 35 to 50 years. Contents of FTN- $\alpha$ , IL-1b, IL-6, IL-6 were studied via method of immune-ferment analysis. Patients with nephrogenic arterial hypertension received zenophenol in dose of 15-30 mg/day, felodipine 10-20 mg/day, or combination of them, depending on a degree of arterial hypertension, as hypertensive therapy. According to recommendations of Worldwide organization of healthcare, the purpose of hypertensive therapy was to achieve target level of arterial pressure (systolic arterial pressure < 14 mm of mercury, diastolic arterial pressure < 90 mm of mercury). Evaluation of indexes of immune state was carried out two times: at the first visit and in 6 months after therapy. Statistic processing of the received data was carried out with programme complex Statistica 8,0 for Windows.

**Results and discussions.** Defining initial level of anti-inflammatory cytokines showed a reliably higher content of them among patients with CGN of the III degree of AH. Among patients of

this group serum concentration of FTN- $\alpha$  was  $4,1 \pm 0,3$  times ( $p < 0,01$ ), IL-1b –  $3,9 \pm 0,5$  times ( $p < 0,01$ ), IL-6 –  $3,5 \pm 0,4$  times ( $p < 0,01$ ) higher than control indexes (FTN- $\alpha$  –  $32,4 \pm 3,6$  pg/ml, IL-1b –  $35,8 \pm 4,1$  pg/ml, IL-6 –  $15,8 \pm 3,9$  pg/ml). Besides, among patients of this group level of FTN- $\alpha$  was  $1,4 \pm 0,2$  times ( $p < 0,05$ ), IL-1b –  $1,5 \pm 1,2$  times ( $p < 0,05$ ), and IL-6 –  $1,4 \pm 0,3$  times ( $p < 0,05$ ) higher than those of patients with CGN of the II degree of AH. Lower serum concentration of the studied cytokines was revealed among patients with the I degree of AH (duration of CGN less than a year). The research results have revealed an increase in content of IL-6 in all analyzed groups of patients. Maximum level of IL-6 ( $1546,2 \pm 11,4$  mg/l) was found in blood serum of patients with CGN of the II degree of AH that was  $1,5 \pm 0,4$  ( $p < 0,05$ ) times higher than this index of the control group ( $1008 \pm 18,3$  mg/l) and exceeded this index of patients with the I and II degree of AH by  $36,5 \pm 1,2\%$  ( $p < 0,05$ ) and  $22,4 \pm 0,8\%$  ( $p < 0,05$ ) correspondingly.

Defining serum concentration of anti-inflammatory cytokines among patients with nephrogenic arterial hypertension against the therapy has provided the following results. Among patients with CGN of the I degree of AH level of anti-inflammatory cytokinemia has decreased significantly. It is proved by the decrease in average concentration of FTN- $\alpha$  –  $2,2 \pm 0,1$  times ( $p < 0,05$ ), IL-1 $\beta$  –  $1,9 \pm 0,2$  times ( $p < 0,05$ ), IL-6 –  $2,1 \pm 0,2$  times ( $p < 0,05$ ); IL-6 –  $1,2 \pm 0,2$  times ( $p < 0,05$ ), compared to the initial data. A similar dynamics of the studied indications was achieved with usage of felodipine without any reliable differences between the compared groups: level of FTN- $\alpha$  decreased  $2,1 \pm 0,2$  times ( $p < 0,05$ ), IL-1 $\beta$  –  $1,7 \pm 0,2$  times ( $p < 0,05$ ), IL-6 –  $2,3 \pm 0,3$  times ( $p < 0,05$ ); IL-6  $1,4 \pm 0,3$  times ( $p < 0,05$ ). The results of therapy with felodipine (20 mg/day) under the II degree of AH showed a decrease in level of FTN- $\alpha$  by  $29,5 \pm 4,5\%$  ( $p < 0,05$ ), IL-1 $\beta$  – by  $30,2 \pm 3,2\%$  ( $p < 0,05$ ), IL-6 – by  $12,6 \pm 2,1\%$  ( $p < 0,05$ ), IL-6 by  $9,8 \pm 1,2\%$  ( $p < 0,05$ ), and did not have any statistic differences with the level of anti-inflammatory cytokinemia that was defined after using preparation zopfenopril (30 mg/day) among patients of a similar group. Prescribing combination of anti-hypertensive preparations felodipine + zopfenopril to patients with CGN of the II group of AH was attended by a significant decrease in anti-inflammatory cytokinemia: level of FTN- $\alpha$  decreased  $2,6 \pm 0,3$  times ( $p < 0,05$ ), IL-1 $\beta$  –  $2,3 \pm 0,2$  times ( $p < 0,05$ ), IL-6 –  $2,6 \pm 0,8$  times ( $p < 0,05$ ), IL-6 –  $1,6$  times ( $p < 0,05$ ). Among patients with the II degree of AH in 6 months after using combination of zenophenopril (30 mg/day) and felodipine (20 mg/day) has shown a reliable decrease in serum concentration of anti-inflammatory cytokines: contents of FTN- $\alpha$  decreased  $1,4 \pm 0,5$  times ( $p < 0,05$ ), IL-1 $\beta$  –  $1,3 \pm 0,3$  times ( $p < 0,05$ ),

IL-6  $-1,4 \pm 0,3$  times ( $p < 0,05$ ), pIL-6p  $-1,4 \pm 0,6$  times ( $p < 0,05$ ).

**Resume.** Contents of anti-inflammatory cytokines in blood serum are increased under hypertensive type of CGN, and it increases along with a severity of arterial hypertension. Zophenopril and felodipine have a similar anti-inflammatory effect under CGN. Using zophenopril in combination with felodipine is attended by an increase in resolving effect of a therapy over inflammatory cytokinemy under hypertensive type of CGN.

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#### DYNAMICS OF CONTENTS OF GROWTH FACTORS, CYTOKINES OF PRO-INFLAMMATORY EFFECT IN SYNOVIAL FLUID AMONG PATIENTS WITH OSTEOARTHRITIS AGAINST THERAPY

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**The objective** of this work is to study an impact of zinaxin upon contents of growth factors: vascular endothelial growth factor A (VEGF-A), fibroblast growth factor (FGF), and pro-inflammatory cytokines (interleukin-1b, IL-1b, IL-6, factor of tumour necrosis  $\alpha$  – FTN- $\alpha$ ) in synovial liquid of patients with osteoarthritis (OA) against treatment with zinaxin.

**Methods and materials.** We have studied 65 patients with OA. Among those – 18 men (27,7%) and 48 women (72,3%). An average age oscillated from 46 to 68 years. Diagnosis OA was established according to diagnostic criterions EULAR (2010). A control group was formed of 20 healthy donors. Synovial liquid for examination was received via puncture of ancles. Level of IL-1b, IL-6, FTN- $\alpha$  was determined by immune-ferment method using test-systems «Protein contour» (Sankt-Petersburg), VEGF-A – by Bender Med systems GmbH (Austria) and FGF – by Biosource GmbH (Belgium). Study of contents of pro-inflammatory cytokines and growth cytokines in synovial liquid among patients with OA was carried out before therapy and in 6 months after treating them with zinaxin. Statistical analysis of the received data was carried out with programme complex Statistica 8,0 for Windows.

**Results and discussions.** The results of defining initial level of pro-inflammatory cytokines in synovial liquid among patients with OA have shown a reliable increase in concentration of IL-1b  $1,8 \pm 0,2$  times ( $p < 0,05$ ), IL-6  $2,2 \pm 0,3$  times ( $p < 0,05$ ), FTN- $\alpha$   $2,3 \pm 0,4$  times ( $p < 0,05$ ),

compared to the control, level of IL-1b in which equaled  $-15,4 \pm 6,1$  pg/ml; IL-6  $-6,2 \pm 1,8$  pg/ml; FTN- $\alpha$   $-32,6 \pm 4,4$  pg/ml. Defining level of VEGF-A in synovial liquid under OA showed an increase in its concentration by  $7,7 \pm 0,7$  ( $p < 0,01$ ), compared to the control ( $15,6 \pm 3,6$  pmole/ml). Within our research we have also studied contents of FGF in synovial liquid of patients with OA that showed an increase in level of FGF  $1,4 \pm 0,3$  times, compared to the control ( $5,1 \pm 0,6$  pg/ml,  $p < 0,05$ ).

Studying dynamics of laboratory indications in 6 months after the taken therapy with zinaxin showed a decrease in average level of: IL-1b – by  $43,8 \pm 1,9\%$  ( $p < 0,05$ ), IL-6 – by  $45,9 \pm 1,4\%$  ( $p < 0,05$ ), FTN- $\alpha$  – by  $35,9 \pm 1,8\%$  ( $p < 0,05$ ), VEGF-A by  $28,4 \pm 1,4\%$  ( $p < 0,05$ ), FGF by  $26,4 \pm 1,2\%$  ( $p < 0,05$ ), compared to the initial data.

**Resume.** An increase in level of pro-inflammatory cytokines (IL-1b, IL-6, FTN- $\alpha$ ) and growth factors (VEGF-A, FGF) in synovial liquid is registered among patients with OA. Zinaxin has a resolving effect over contents of IL-1b, IL-6, FTN- $\alpha$ , VEGF-A, FGF in synovial liquid among patients with osteoarthritis.

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#### CEREBRAL MICROBLEEDS AS A MARKER SEVERITY CEREBROVASCULAR AND NEURODEGENERATIVE DISEASES WITH COGNITIVE IMPAIRMENT

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The aim of the study was to determine the location and number of CMB in patients with cerebrovascular and neurodegenerative diseases (Alzheimer's disease and dementia with Lewy bodies) and to study the contribution CMB and accompanying vascular changes of the brain on the cognitive impairment. We observed 48 patients (mean age 73,3 years, 29 (60%) male) by means MR tomograph and neuropsychological methods. The total number of patients with CMB were 40% (19 patients). The total number of CMB – 220, of which 161 cortical localization. Of the 23 patients with AD, 10 (44%) patients had occipital cortical CMB (65%) and parietal (19%) localization. Most CMB 202 (92%) was observed in patients with leukoencephalopathy Fazekas 3 point (high) when they were accompanied by severe atrophy of the hippocampus. Thus, vascular process is universal and additional negative factor inducing different clinical forms of dementia.