IL-6 –1,4 ± 0,3 times ($p < 0,05$), pIL-6p – 1,4 ± 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 felodipne 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.

The work was submitted to International Scientific Conference «Fundamental and applied research in medicine», France (Paris), 14-21, October, 2012, came to the editorial office on 18.10.2012.

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

Knyazeva L.A., Brezhneva I.N., Goryainov I.I., Lukashov A.A., Maltseva G.I.

Kursk state medical university, Kursk, e-mail: kafedra_n1@bk.ru

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 α – FTN-α) 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. LevelofIL-1b, IL-6, FTN-α wasde fined byaimmune-fermenine method using test-systems «Protein contour» (Sankt-Petersburg), VEGF-A – by Bender Med systems Gmbh (Austria) andFGF – 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 ± 0,2 times ($p < 0,05$), IL-6 2,2 ± 0,3 times ($p < 0,05$), FTN-α 2,3 ± 0,4 times ($p < 0,05$), compared to the control, level of IL-1b in which equaled – 15,4 ± 6,1 pg/ml; IL-6 – 6,2 ± 1,8 pg/ml; FTN-α – 32,6 ± 4,4 pg/ml. Defining level of VEGF-A in synovial liquid under OA showed an increase in its concentration by 7,7 ± 0,7 ($p < 0,01$), compared to the control (15,6 ± 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 ± 0,3 times, compared to the control (5,1 ± 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 ± 1,9% ($p < 0,05$), IL-6 – by 45,9 ± 1,4% ($p < 0,05$), FTN-α – by 35,9 ± 1,8% ($p < 0,05$), VEGF-Aby 28,4 ± 1,4% ($p < 0,05$), FGF by 26,4 ± 1,2% ($p < 0,05$), compared to the initial data.

Resume. An increase in level of pro-inflammatory cytokines (IL-1b, IL-6, FTN -α) 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-α, VEGF-A, FGF in synovial liquid among patients with osteoarthritis.

The work was submitted to International Scientific Conference «Fundamental and applied research in medicine», France (Paris), 14-21, October, 2012, came to the editorial office on 18.10.2012.

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

Makotrova T.A., Vasenina E.E., Levin O.S., Arablinskiy A.V.

Russian Medical Academy of Postgraduate Education, Moscow; Clinical Hospital of S.P. Bodkin, Moscow, e-mail: tatianamak86@gmail.com

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.

Abbreviations
CMB – cerebral microbleeds
MRI – magnetic resonance imaging
CAA – cerebral amyloid angiopathy
AD – Alzheimer's disease

Introduction. Cerebral microbleeds (CMB) are defined as small round hypointense spots on T2* – weighted gradient-recalled echo (GRE) magnetic resonance imaging (MRI) and are believed to represent hemosiderin deposits that can remain in macrophages for years following a microhemorrhage. CMB can be detected in cerebral microangiopathy of different origins: cerebral amyloid angiopathy and hypertensive arteriopathy.

Cerebral amyloid angiopathy (CAA) – a disease of leptomeningeal and cortical arteries of the brain, characterized by the deposition of amyloid in the vessel walls of small arteries and capillaries (media and adventitia). The amyloid changes the architecture of the vascular wall up to the formation of a «vessel in vessel» and microaneurysms, in addition to the vessel wall is marked fibrinoid necrosis, hyaline degeneration of the vessels with the lumen obliteration. Amyloid deposits are distributed irregularly. The cortical arteries are affected mainly, especially in the occipital lobes. CAA can be an independent disease, but is often combined with Alzheimer's disease (AD).

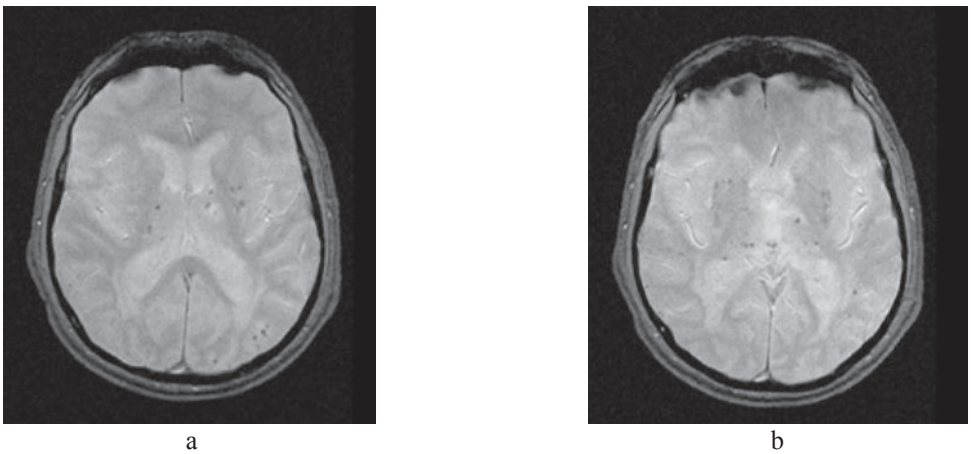
Based on various sites CMBs in neurodegenerative and cerebrovascular diseases we can view CMB for differential diagnostic value. Thus, cortical CMB were observed in cerebral amyloid angiopathy and deep CMB were observed in hypertensive microangiopathy.

MRI plays a central role in the diagnosis of CMB. MRI T2-weighted sequences*-gradient echo (GRE) is an opportunity to find the «old» and «fresh» CMB, observed in this mode as gipointensivnyh spots, and can not be seen using other imaging techniques.

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.

Materials and methods. We observed 48 patients (mean age 73,3 years, 29 (60%) male) with cerebrovascular and neurodegenerative diseases with cognitive impairment on the basis of clinical hospital named S.P. Botkin, Moscow. MRI was performed on a MR tomograph with a magnetic field of 1,5 Tesla «Signa Excite» company GE (USA, 2006), the thickness of the slice gwas 5 mm. To assess the associated changes were used visual Fazekas scale (Fazekas, 1998) and Sheltens (Scheltens). CMB were analyzed with mapping microbleeds anatomical rating scale (MARS) (Gregoire SM, 2009) and rating scale brain microbleeds (BOMBS). Neuropsychological testing included Montreal Cognitive Assessment scale (MoCA), Addenbrooke's Cognitive Examination (ACE-R), Clock Drawing Test, fluency test, visual memory test (SCT).

Results. 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. Patients with cerebrovascular disease had deep (subcortical) CMB only in cases of severe vascular leukoencephalopathy 2-3 points (7 cases, 64%). Most CMB 202 (92%) was observed in patients with leukoencephalopathy Fazekas 3 point (high) when they were accompanied by severe atrophy of the hippocampus. Patients with CMB had significantly lower scores of memory (by 2,1 points), attention (2,9), and visual-spatial functions (3,9) of neuropsychological profile than patients without CMB (Fisher's exact test $P < 0,01$).



a b

Example of 72-year-old patient with symptomatic Alzheimer's disease and cerebrovascular disease with multiple cortical (a) and deep (a, b) CMBs (axial images 1,5 T MRI T2*-weighted images GE)

Conclusions. Based on the obtained results it can be concluded that the vascular process is universal and additional negative factor inducing different clinical forms of dementia. Cognitive decline in patients with cerebrovascular disease and cerebral amyloid angiopathy associated with numerous CMB with 1,5 Tesla MRI, but the multiple CMB is an independent predictor of cognitive decline.

References

1. Gregoire S.M. Smith K. Jäger H.R. Cerebral Microbleeds and Long-Term Cognitive Outcome: Longitudinal Cohort Study of Stroke Clinic Patients // Cerebrovasc Dis. – 2012. – № 33. – P. 430–435.

2. Auriel E., Greenberg S.M. The Pathophysiology and Clinical Presentation of Cerebral Amyloid Angiopathy // Curr Atheroscler Rep. – 2012.

3. Jacques De Reuck, Vincent Deramecourt, Charlotte Cordonnier. Prevalence of small cerebral bleeds in patients with a neurodegenerative dementia: A neuropathological study // Journal of the Neurological Sciences. – 2011. – № 300. – P. 63–66.

4. Werring D.J., Gregoire S.M., Cipolotti L. Cerebral microbleeds and vascular cognitive impairment // J Neurol Sci. – 2010. – № 299. – P. 131–5.

The work was submitted to International Scientific Conference «Fundamental and applied research in medicine», France (Paris), 14-21, October, 2012, came to the editorial office on 30.10.2012.

ESTIMATION OF NORMAL NITROTYROSINE LEVEL IN HUMAN BLOOD PLASMA

Martusevich A.K., Soloveva A.G., Didenko N.V.

Nizhny Novgorod Research Institute of Traumatology and Orthopaedics, Nizhny Novgorod, e-mail: cryst-mart@yandex.ru

Now a day many papers are dedicated to investigation of oxidative stress as a main pathogenesis component of different human diseases [1]. This pathological state is associated with misbalance between lypoperoxidation intensity and antioxidant reserves. On the other hand oxidative stress mechanisms include some additional substances, such as nitrosative stress products, lipids and chlorine-contained bioradicals, but pathological and physiological role of these components are not studied fully [2, 3]. In addition, there on many informative methods and parameters, estimating level of oxidative and nitrosative stress.

Nitrotyrosine, forming as result of nitroxylation of blood proteins and oligopeptides, is the one of stable end products of nitrosative stress [3]. That is why this parameter can be its informative laboratory marker, but real physiological level of investigated substance is discussed [1-3].

The *aim of this paper* is estimation of nitrotyrosine concentration in blood plasma of healthy people.

Material and methods. We studied samples of conserved blood serum of 15 healthy people (blood donors). Estimation of nitrotyrosine level was executed with special ELISA kit (Hycult Biotech) [2]. Spectrophotometric investigations were carried out with «PowerWave XS» apparatus (USA). From the experiment moment donors' blood plasma was stored at standard refrigerator temperature (0-4 °C). Refreezing of blood samples was accomplished with typical protocol during 2,5-3 hours. Calibration curve was founded by use of standard calibration procedure with diluted testing solution for rated formula getting. Final level of blood serum nitrotyrosine was calculated with last one.

Statistic processing of the data was accomplished by the programs Microsoft Excel 2003 and Primer of Biostatistics 4.03. The descriptive statistics data is shown in the article.

Results. It was stated, that physiological plasma concentration of nitrotyrosine in blood serum of healthy people is 9,38 ± 2,69 nM. This parameter reference interval in from 5,13 to 14,5 nM. These data from our experiments can refine published information about physiological interval, including 3-40 nM plasma nitrotyrosine as normal level [2]. Indicated specialties of substance level may be caused by used preservative.

It is interesting, that there are two groups of patients with low (over 5 nM) and high (over 13,5 nM) level of blood serum nitrotyrosine. We supposed there are different nitroxylation level of tyrosine and tyrosine-contained proteins in blood plasma of healthy people. It can be associated with various concentrations substrates for nitrogen reactive species effect.

Conclusion. So, nitrotyrosine level in blood plasma of healthy human is very low, but it illustrates presence of nitroxylation processes in investigated biological substrate under physiological conditions. On our opinion, registration of plasma nitrotyrosine level can be a marker of nitrosative stress in vitro and in vivo. Different agents (exogenic nitric oxide, some prooxidants etc.) or pathological conditions (intoxication, metabolic disorders, traumas and others) may caused stimulation of nitroxylation processes in vivo, leading to NO-dependent molecular and cellular damage without compensation mechanisms.

References

1. Sajdel-Sulkowska E. et al. Potential role of oxidative stress in mediating of the effect of altered gravity on the developing rat cerebellum // Adv. Space Res. – 2007. – Vol. 40. – P. 1414-1420.

2. ter Steege J. et al. Nitrotyrosine in plasma of celiac disease patients as detected by a new sandwich ELISA // Free Rad. Biol. Med. – 1998. – Vol. 25. – P. 953.

3. Whiteman M. et al. Lack of tyrosine nitration by hypochlorous acid in the presence of physiological concentrations of nitrite. Implication for the role of nitryl chloride in tyrosine nitration in vivo // J. Biol. Chem. – 2003. – Vol. 278. – P. 8380.

The work was submitted to International Scientific Conference «Innovative medical technologies», Russia (Moscow), 20-22, November, 2012, came to the editorial office on 18.10.2012.