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Increased visinin-like protein-1, YKL-40, lipocalin-2, and IL-23 levels in patients with migraine

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ABSTRACT

Background: Migraine is a type of primary headache caused by changes in the trigeminal system and has been reported to be associated with neurovascular inflammation of cerebral and extracerebral vessels.

Objective: It is known that inflammation is an important process in the pathogenesis of migraine. It has been shown that the molecules of visinin-like protein 1 (Vilip-1), YKL-40, lipocalin-2 and interleukin (IL)-23 play a role in the inflammatory process. Our aim is to investigate the role of this molecule in the metabolic pathway of migraine disease.

Methods: Fifty migraine patients with and without aura in the interictal period were included in the study. Vilip-1, YKL-40, lipocalin-2, and IL-23 levels were measured by ELISA method.

Results: Serum vilip-1, YKL-40, lipocalin-2, and IL-23 levels were found to be significantly higher in migraine patients compared to the control group. We found that this molecule increased significantly in migraine subgroups compared to the control group ($p < 0.001$). A positive significant correlation was found between vilip-1 level and YKL-40 and lipocalin-2 levels in migraine patients. In addition, a positive correlation was observed between visual analogue scale score, number of days with pain and vilip-1 level ($p < 0.01$). The results of our study showed that activation of inflammatory mediators may play a role in the pathogenesis of migraine disease. In addition, our study is valuable in that inflammatory molecules are high in the interictal period and these biomarkers have never been analyzed in migraine patients. However, we still believe that larger studies are needed to explain the role of vilip-1, YKL-40, lipocalin-2, and IL-23 in the molecular mechanism of migraine disease.

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Introduction

Migraine is a type of primary headache caused by changes in the trigeminal system and is known to be associated with neurovascular inflammation of cerebral and extra-cerebral vessels [1]. The pathophysiological mechanism of migraine disease is complex and has not been fully explained. Activation of mast cells, stimulation of trigeminal nerves, calcitonin gene-related peptide, stimulation of dural vessels, secretion of molecules such as substance P and neurokinin A are considered among the etiological factors of migraine [2,3].

Visinin-like protein-1 (Vilip-1) is a neuronal calcium-sensor protein reported to be increased in the cerebrospinal fluid (CSF) after stroke. Therefore, it has been identified as a sign of neuronal damage [4]. It has been reported that vilip-1 molecule plays an active role in the pathophysiology of central nervous system (CNS) diseases such as schizophrenia and Alzheimer's disease [5]. YKL-40 is a member of the mammalian chitinase-like protein family [6]. The function of YKL-40 has not been fully explained. As an inflammatory glycoprotein, it is thought to be involved in many pathophysiological processes, such as cell proliferation, migration, and chemotaxis [7,8]. It has been reported that the level of YKL-40 is elevated in the CSF in infectious and non-infectious CNS diseases [9]. In addition, it has been reported that serum YKL-40 levels are increased in CSF of Alzheimer's patients and multiple sclerosis (MS) disease [10,11].

Interleukin (IL)-23 is secreted by activated macrophages and dendritic cells in peripheral tissues, including the skin, intestinal mucosa and lungs [12]. It has been reported that the level of IL-23 is increased in inflammatory diseases such as rheumatoid arthritis, psoriasis and inflammatory bowel disease [13]. Lipocalin-2 synthesized from adipose tissue and liver plays a role in various cellular events, immune response, differentiation and tumorigenesis [14]. It has been reported that the lipocalin-2 molecule plays an active role in chronic diseases such as neurodegenerative diseases [15].

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No studies have been found in the literature related to biomarkers and migraine disease. Therefore, our aim is to evaluate the relationship of vilip-1, YKL-40, lipocalin-2 and IL-23 biomarkers with the molecular mechanism of migraine.

Methods

Our study was carried out in Dicle University Faculty of Medicine, Department of Neurology. The migraine patients were clinically assessed by a neurologist. This study was approved by the ethics committee of Dicle University (18.05.2018/175), and written informed consent was obtained from all participants prior to their inclusion into the study migraine diagnosis was carried out in accordance with the international classification of headache disorders-III diagnostic criteria [16]. The patients in the migraine group were divided into two subgroups. It was determined that only 50 patients had migraines without aura, while the remaining patients all had migraine with aura. The exclusion criteria of the study were as follows: diabetes, thyroid dysfunction, pregnancy, cardiovascular diseases, chronic illnesses, renal diseases, infectious diseases and metabolic diseases.

Biochemical analyses

Blood samples were taken from the control group and from the migraine group. The venous blood samples were instantaneously centrifuged at 3000 rpm for 10 min at 4°C and then poured into an eppendorf tube. The serum samples were transferred on ice and stored at −80°C for 3 months until the end of the study. The serum vilip-1, YKL-40, lipocalin-2, and IL-23 levels were measured using commercially available enzyme-linked immunosorbent assay (ELISA) kits (YLbiont, Kit LTD, China). The absorbance was read at 450 nm and recorded by absorbance microtiter plate reader (ELx800TM, BIO-TEK instruments, USA).

Statistical analysis

Compliance of the data with normal distribution was checked with Kolmogorov – Smirnov and Shapiro–Wilk tests. Student – t test was used for groups of two, One Way ANOVA for groups of three for parameters that were normally distributed, Mann Whitney-U test was used for comparison of paired groups for parameters not normally distributed, and Kruskal Wallis test was used for comparison of more than two groups. In comparison with the Kruskal–Wallis test, two-fold comparisons were made with the Mann-Whitney-U test by making Bonferroni correction to understand which group caused the statistical difference.

Results

The mean age of the migraine with aura (39 females and 11 males) 28.60 ± 8.12 and migraine without aura (35 females and 15 males) was 28.44 ± 8.16 years, while the mean age of the control group (29 females and 21 males) was 27.70 ± 7.17 years (Table 1).

The mean serum vilip-1 levels of in patients with migraine and healthy individuals were 4.43 ± 3.94 ng/ml, 2.32 ± 3.29 ng/ml, respectively. The mean serum YKL-40 levels of in patients with migraine and healthy individuals were 36.40 ± 28.73 pg/ml, 18.45 ± 10.23 ng/ml, respectively. The mean serum lipocalin-2 levels of in patients with migraine and healthy individuals were 429.03 ± 253.34 pg/ml, 228.02 ± 108.15 ng/ml respectively. The mean serum IL-23 levels of in patients with migraine and healthy individuals were 70.39 ± 57.09 ng/ml, 30.16 ± 13.39 ng/ml, respectively. The serum IL-23, YKL-40, lipocalin-2, and vilip-1 levels were found to be higher in the migraine patients compared to the control group. This difference was found to be statistically significant compared ($p < 0.001$) Table 2.

In migraine with aura and migraine without aura, serum IL-23, YKL-40, lipocalin-2, and vilip-1 levels were significantly higher than in the control group ($p < 0.001$). However, no significant difference was

Table 1. The demographic values of the migraine subgroups and control group.

	Control group	Migraine without aura	Migraine with aura
Female	29(58.0%)	35(70.0%)	39(78.0%)
Male	21(42.0%)	15(30.0%)	11(22.0%)
Age	27.70 ± 7.17	28.44 ± 8.16	28.60 ± 8.12
BMI	23.29 ± 4.41	24.40 ± 4.48	24.40 ± 4.48

Table 2. Baseline characteristics serum visinin-like protein-1, YKL-40, lipocalin-2, and IL-23 levels in patients with migraine and control group.

Parameters	Control group	Migraine group	Lower Bound	Upper Bound	p value
Vilip-1(ng/mL)	2.32 ± 3.29	4.43 ± 3.94*	0.765	0.917	**.000**
YKL-40 (ng/mL)	18.45 ± 10.23	36.40 ± 28.73*	0.743	0.907	**.000**
Lipocalin-2 (ng/L)	228.02 ± 108.15	429.03 ±253.34*	0.737	0.886	**.000**
IL-23(ng/L)	30.16 ± 13.39	70.39 ± 57.09*	0.735	0.880	**.000**

Data are expressed as (mean ± SD) SD; Standard Deviation.
$p < 0.001$*. the degree of significance of comparison between the patient and control group.

Table 3. Comparison of serum visinin-like protein-1, YKL-40, lipocalin-2, and IL-23 levels of migraine subgroups and control group.

Parameters	Control group	Migraine without aura	Migraine with aura	p value
Vilip-1 (ng/mL)	2.32 ± 3.29	5.43 ± 4.38	3.42 ± 3.16	**.000**
YKL-40 (ng/mL)	18.45 ± 10.23	35.47 ± 28.58	37.32 ± 29.14	**.000**
Lipocalin-2 (ng/L)	228.02 ± 108.15	421.59 ± 312.65	436.48 ± 178.35	**.000**
IL-23 (ng/L)	30.16 ± 13.39	54.59 ± 38.95	86.20 ± 67.52	**.000**

Data are expressed as (mean ± SD) SD; Standard Deviation.
*p < 0.001**. the degree of significance of comparison between the patient and control group.

Table 4. The number of days with pain, duration of pain and MIDAS and VAS score values of the patients.

	Migraine without aura	Migraine with aura	p value
Days with pain	9.34±198	7.02±1.87	**.000**
VAS Scores	6.40±0.90	4.52±1.16	**.000**
Duration of pain	8.98±3.73	6.42±2.39	**.000**
MIDAS	7.12±2.69	6.06±2.45	.088

Data are expressed as (mean ± SD) SD; Standard Deviation.
p < 0.001*, the degree of significance of comparison between the patient and control group.
MIDAS, Migraine Disability Assessment Test; VAS, Visual Analogue Scale scores.

found between migraine with aura and without aura groups (p > 0.05) Table 3.

Days with pain, duration of pain, and visual analogue scale score (VAS) values were statistically higher migraine without aura group than the migraine with aura (p < 0.001). Migraine disability assessment test was not statistically (p > 0.05) Table 4.

A cutoff YKL-40 of 45.25 predicted the difference between the migraine group and the control group, with 23% sensitivity and 98% specificity (ROC area under the curve [AUC] of 0.82 95% confidence interval [CI], 0.743–0.907. A cutoff vilip-1 of 3.03 predicted the difference between the migraine group and the control group, with 47% sensitivity and 92% specificity (ROC AUC of 0.84 95% [CI] 0.765–0.917). A cutoff lipocalin-2 of 523.44 predicted the difference between the migraine group and the control group, with 23% sensitivity and 98% specificity (ROC AUC of 0.81 95% [CI] 0.737–0.886). A cutoff IL-23 of 58.81 predicted the difference between the migraine group and the

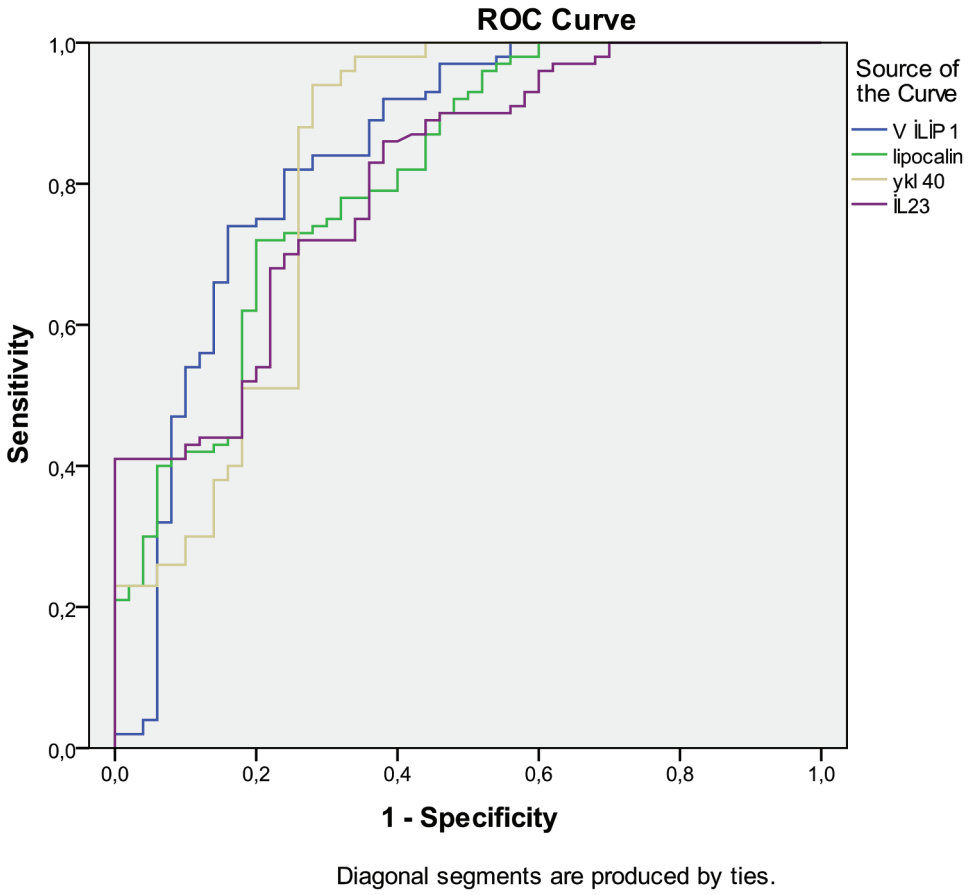

Figure 1. The Receiving Operator Characteristic (ROC) curve analysis of visinin-like protein-1, YKL-40, lipocalin-2, and IL-23 for prediction the migraine patient group.

control group, with 41% sensitivity and 98% specificity (ROC AUC of 0.80 95% [CI] 0.735–0.880 (Figure 1).

Discussion

In our study, we found that serum YKL-40, IL-23, lipocalin-2 and vilip-1 levels were increased in migraine patients. We found that this molecule increased significantly in migraine patients with and without aura compared to the control group. A significant correlation was found between vilip-1 levels and YKL-40 and lipocalin-2 levels. A positive correlation was observed between VAS score, number of days with pain and serum vilip-1.

YKL-40, IL-23, lipocalin-2 and vilip-1 molecules have never been measured in migraine patients. Therefore, the mechanism of this molecule in the pathogenesis of migraine disease has not been explained. Our study is the first clinical study to bring innovation to the literature with this aspect.

Vilip-1 is a neuron-specific calcium sensor (NCS) protein expressed in the central nervous system [17]. NCS proteins are localized in the central nervous system such as retinal photoreceptor neurons or neuroendocrine cells [18]. Calcium plays an important role in neuron physiology homeostasis [19]. Therefore, vilip-1 has been used as a biomarker for the identification of neuronal damage. It has been reported that plasma vilip-1 level plays an active role in stroke patients [20]. It has been reported to alter calcium homeostasis in migraine [21]. Therefore, calcium overload causes persistently increased cytosolic Ca^{2+} concentrations in neurons. In this case, it has been stated that it causes the involvement of NCS proteins in the CNS, which mediates various necrotic and apoptotic pathways [22]. The high vilip-1 level in our study suggests that calcium may disrupt homeostasis and cause neuron excitability and this molecular mechanism may cause migraine headaches. In addition, the positive correlation between the YKL-40 and lipocalin-2 biomarkers and vilip-1 levels indicates that vilip-1 molecule may play a role in the inflammatory process of migraine.

YKL-40 is expressed in microglia [23]. YKL-40 is synthesized and secreted by cells, such as macrophages, hepatic stellate cells, smooth muscle cells, neutrophils, and chondrocytes. Many studies have been carried out in the literature with YKL-40. It has been reported that YKL-40 plays a role in some inflammatory diseases and in the development of atherosclerosis [24]. YKL-40 has been reported to play a role in the etiopathogenesis of MS patients and neurodegenerative diseases [25]. It has been reported that YKL-40 neuron expression is increased in the experimental model of status epilepticus [26]. Therefore, YKL-40 has been shown to be a potential biomarker in inflammatory diseases. In our study, serum YKL-40 was significantly increased in migraine patients. The elevation of the glial marker YKL-40 in migraine patients indicates the presence of neurovascular inflammation in the pathogenesis of migraine.

Lipocalin-2 is known to play a role in inflammatory responses in the CNS [27]. Lipocalin-2 Alzheimer's disease experimental autoimmune encephalomyelitis (EAE) has been shown to play an effective role in neurological diseases with many neuroinflammation disease pathogenesis [28,29]. Lipocalin-2 is a protein secreted in inflammatory events by activated astrocytes in the brain after the stroke [30]. In our study, lipocalin-2 level was found to be significantly higher in migraine patients. It was also observed that it was higher in migraine subgroups. High lipocalin-2 level in migraine etiopathogenesis indicates inflammation. Therefore, it is suggested that lipocalin-2 may cause microglial cell activation in the pathophysiology of migraine, and as a result, neurovascular inflammation may occur by this molecular mechanism by affecting vascular permeability [31].

IL-23 is a covalent heterodimer of IL-12p40 and IL-23p19 [32]. IL-23 is a cytokine produced by dendritic cells and infiltrating macrophages from brain injury and is a molecule involved in the pathogenesis of autoimmune and inflammatory diseases [33]. Numerous studies have been conducted showing the role of IL-23 in neuroinflammation. It has been reported that IL-23 mRNA expression is increased in MS patients [34]. IL-23 has been reported to aggravate neuron damage, astrocyte swelling and disrupt the blood–brain barrier integrity [35]. Elevated serum IL-23 levels have been reported after an ischemic stroke [36]. It has been reported that IL-23/IL-17A metabolic pathway plays an important role in the pathogenesis of Alzheimer's disease [37]. Cua et al. demonstrated that IL-23 plays an important role in autoimmune inflammation of the CNS [38]. In our study, IL-23 level was found to be significantly higher in migraine patients. In addition, it was observed that it was higher in migraine patients with and without aura than in the control group. In the light of this information, high levels of IL-23 in migraine patients indicate that it may be caused by microglial activity by activating T cells. In addition, the sensitivity of our YKL-40, IL-23, lipocalin-2 and vilip-1 tests was found to be very low due to the low area under the ROC curve, but the likelihood ratios were found to be good.

Many studies have been conducted on cytokines and in the attack and interictal period of migraine patients. It has been reported that pro-inflammatory molecules such as IL-1β, IL-6, TNF-α are increased in the interictal period [39]. Yücel et al. reported that molecules such as ESM-1, CLDN-5, IL-1β, and IL-6 are elevated in the attack and interictal period [40]. In our study, serum YKL-40, IL-23, lipocalin-2 and vilip-1 levels were significantly increased in the interictal

period. The data we obtained in our study were found to be compatible with the literature. The elevation of these molecules in the interictal period may be an indicator of neurogenic inflammation. In addition, in our study, there was a positive correlation between VAS score, number of days with pain and serum vilip-1. In this sense, it is thought that large-scale studies will increase therapeutic approaches to migraine disease.

In conclusion, in our study, it was determined that vilip-1, YKL-40, lipocalin-2 and IL-23 were levels increased in migraine patients. Therefore, the results of our study draw attention to the inflammation process in the pathophysiology of migraine. In addition, the fact that these biomarkers are significantly higher in migraine patients with aura and that they have never been studied in migraine patients makes our study valuable. There is a need for more extensive studies to support our work in this regard.

Disclosure statement

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Authors' contributions

The authors contributed equally to data collection, methodology, literature review, material collection, statistical analysis, data evaluation, article writing, editing.

References

[1] Hamed SA. The vascular risk associations with migraine: relation to migraine susceptibility and progression. Atherosclerosis. 2009 Jul;205(1):15–22.
[2] Martins LB, Duarte H, Ferreira AV, et al. Migraine is associated with altered levels of neurotrophins. Neurosci Lett. 2015;587:6–10.
[3] Ward TN. Migraine diagnosis and pathophysiology. Continuum (Minneap Minn). 2012;18(4):753–763.
[4] Scheff SW, Price DA, Ansari MA, et al. Synaptic change in the posterior cingulate gyrus in the progression of Alzheimer's disease. J Alzheimers Dis. 2015;43(3):1073–1090. DOI:10.3233/JAD-141518
[5] Braunewell K, Riederer P, Spilker C, et al. Abnormal localization of two neuronal calcium sensor proteins, visinin-like proteins (vilips)-1 and -3, in neocortical brain areas of Alzheimer disease patients. Dement Geriatr Cognit Disord. 2001 Mar-Apr;12(2):110–116.
[6] Rehli M, Krause SW, Andreesen R. Molecular characterization of the gene for human cartilage gp-39 (CHI3L1), a member of the chitinase protein family and marker for late stages of macrophage differentiation. Genomics. 1997;43(2):221–225.
[7] Johansen JS, Schultz NA, Jensen BV. Plasma YKL-40: a potential new cancer biomarker? Future Oncol. 2009;5(7):1065–1082.
[8] Nishikawa KC, Millis AJ. gp38k (CHI3L1) is a novel adhesion and migration factor for vascular cells. Exp Cell Res. 2003;287(1):79–87.
[9] Prakash M, Bodas M, Prakash D, et al. Diverse pathological implications of YKL-40: answers may lie in 'outside-in' signaling. Cell Signal. 2013 Jul;25(7):1567–1573.
[10] Rosen C, Andersson CH, Andreasson U, et al. Increased levels of chitotriosidase and YKL-40 in cerebrospinal fluid from patients with Alzheimer's disease. Dement Geriatr Cogn Dis Extra. 2014;4:297–304.
[11] Dönder A, Özdemir HH. Serum YKL-40 levels in patients with multiple sclerosis. Arq Neuropsiquiatr. 2021 Sep;79(9):795–798.
[12] McKenzie BS, Kastelein RA, Cua DJ. Understanding the IL-23-IL-17 immune pathway. Trends Immunol. 2006 Jan;27(1):17–23.
[13] Tang C, Chen S, Qian H, et al. Interleukin-23: as a drug target for autoimmune inflammatory diseases. Immunology. 2012 Feb;135(2):112–124.
[14] Choi KM, Lee JS, Kim EJ, et al. Implication of lipocalin-2 and visfatin levels in patients with coronary heart disease. Eur J Endocrinol. 2008 Feb;158(2):203–207.
[15] Dekens DW, Naudé PJ, Engelborghs S, et al. Neutrophil gelatinase-associated lipocalin and its receptors in Alzheimer's Disease (AD) brain regions: differential Findings in AD with and without depression. J Alzheimers Dis. 2017;55(2):763–776. DOI:10.3233/JAD-160330
[16] Headache Classification Committee of the International Headache Society (IHS) the International Classification of Headache Disorders 3rd edition (beta version). Cephalalgia. 2013 Jul;33(9):629-808. doi:10.1177/0333102413485658 doi: doi: doi: . doi: ed.
[17] Braunewell KH, Klein-Szanto AJ. Visinin-like proteins (VSNLs): interaction partners and emerging functions in signal transduction of a subfamily of neuronal Ca2+ -sensor proteins. Cell Tissue Res. 2009 Feb;335(2):301–316.
[18] Ames JB, Ishima R, Tanaka T, et al. Molecular mechanics of calcium-myristoyl switches. Nature. 1997 Sep 11;389(6647):198–202.
[19] Bezprozvanny I. Calcium signaling and neurodegenerative diseases. Trends Mol Med. 2009 Mar;15(3):89–100.
[20] Tarawneh R, Ford AL, Ohlendorf M, et al. Visinin-like protein-1 (VILIP- 1): a novel plasma biomarker for the detection of acute cortical ischemic stroke. Stroke. 2011;42:E203–1203.
[21] Gargus JJ. Genetic calcium signaling abnormalities in the central nervous system: seizures, migraine and autism. Ann N Y Acad Sci. 2009 Jan;1151:133–156.
[22] Blandini F, Braunewell KH, Manahan-Vaughan D, et al. Neurodegeneration and energy metabolism: from chemistry to clinics. Cell Death Differ. 2004 Apr;11(4):479–484.
[23] Bonneh-Barkay D, Bissel SJ, Wang G, et al. YKL-40, a marker of simian immunodeficiency virus

encephalitis, modulates the biological activity of basic fibroblast growth factor. Am J Pathol. 2008 Jul;173 (1):130–143.
[24] Erzin Y, Uzun H, Karatas A, et al. Serum YKL-40 as a marker of disease activity and stricture formation in patients with Crohn's disease. J Gastroenterol Hepatol. 2008 Aug;23(8 Pt 2):e357–62.
[25] Villar-Piqué A, Schmitz M, Hermann P, et al. Plasma YKL-40 in the spectrum of neurodegenerative dementia. J Neuroinflammation. 2019 Jul 12;16(1):145.
[26] Long X, Hu H, Li S, et al. Hippocampal YKL-40 expression in rats after status epilepticus. Epilepsy Res. 2016 Sep;125:52–57.
[27] Kang SS, Ren Y, Liu CC, et al. Lipocalin-2 protects the brain during inflammatory conditions. Mol Psychiatry. 2018 Feb;23(2):344–350.
[28] Dekens DW, Naudé PJW, Keijser JN, et al. Lipocalin 2 contributes to brain iron dysregulation but does not affect cognition, plaque load, and glial activation in the J20 Alzheimer mouse model. J Neuroinflammation. 2018 Nov 30;15(1):330.
[29] Nam Y, Kim JH, Seo M, et al. Lipocalin-2 protein deficiency ameliorates experimental autoimmune encephalomyelitis: the pathogenic role of lipocalin-2 in the central nervous system and peripheral lymphoid tissues. J Biol Chem. 2014 Jun 13;289(24):16773–89.
[30] Lee S, Jha MK, Suk K. Lipocalin-2 in the inflammatory activation of brain astrocytes. CritRevImmunol. 2015;35(1):77–84.
[31] Goadsby PJ, Knight YE, Hoskin KL, et al. Stimulation of an intracranial trigeminally-innervated structure selectively increases cerebral blood flow. Brain Res. 1997 Mar 21;751(2):247–252.
[32] Oppmann B, Lesley R, Blom B, et al. Novel p19 protein engages IL-12p40 to form a cytokine, IL-23, with biological activities similar as well as distinct from IL-12. Immunity. 2000 Nov;13(5):715–725.
[33] Gelderblom M, Arunachalam P, Magnus T. γδ T cells as early sensors of tissue damage and mediators of secondary neurodegeneration. Front Cell Neurosci. 2014 Nov 5;8:368. DOI:10.3389/fncel.2014.00368.
[34] Krakauer M, Sorensen P, Khademi M, et al. Increased IL-10 mRNA and IL-23 mRNA expression in multiple sclerosis: interferon-beta treatment increases IL-10 mRNA expression while reducing IL-23 mRNA expression. Mult Scler. 2008 Jun;14 (5):622–630.
[35] Wang M, Zhong D, Zheng Y, et al. Damage effect of interleukin (IL)-23 on oxygen-glucose-deprived cells of the neurovascular unit via IL-23 receptor. Neuroscience. 2015 Mar 19;289:406–416.
[36] Backes FN, de Souza A, Bianchin MM. IL-23 and IL-17 in acute ischemic stroke: correlation with stroke scales and prognostic value. Clin Biochem. 2021 Dec;98:29–34.
[37] Mohammadi Shahrokhi V, Ravari A, Mirzaei T, et al. IL-17A and IL-23: plausible risk factors to induce age-associated inflammation in Alzheimer's disease. Immunol Invest. 2018 Nov;47(8):812–822.
[38] Cua DJ, Sherlock J, Chen Y, et al. Interleukin-23 rather than interleukin-12 is the critical cytokine for autoimmune inflammation of the brain. Nature. 2003 Feb 13;421(6924):744–748.
[39] Fidan I, Yüksel S, Ymir T, et al. The importance of cytokines, chemokines and nitric oxide in pathophysiology of migraine. J Neuroimmunol. 2006 Feb;171 (1–2):184–188.
[40] Yücel M, Kotan D, Gurol Çiftçi G, et al. Serum levels of endocan, claudin-5 and cytokines in migraine. Eur Rev Med Pharmacol Sci. 2016 Mar;20(5):930–936.