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The role of interleukin-10 and its encoding gene polymorphism influence on the course of infections caused by varicella-zoster virus

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The purpose is to find out the role of changes in the quantitative content of IL-10 in association with the polymorphism of gene encoding it (rs 1800872) in the course of chickenpox and herpes zoster.

Materials and methods. The study included 50 adult patients with chicken pox and 50 patients with herpes zoster. The analysis of the quantitative serum content of IL-10 depending on the genetic polymorphism of this cytokine (rs 1800872) and the effect on the disease course was carried out. The quantitative serum content of IL-10 was determined by enzyme immunoassay, the determination of single nucleotide polymorphism of IL-10 (rs 1800872) in whole venous blood of patients was performed by real-time polymerase chain reaction. The control group consisted of 40 healthy individuals. Statistical data processing was performed using the existing patient database with the application of Statistica for Windows 13 program (StatSoft Inc., No JPZ804I382130ARCN10-J).

Results. The TT genotype of the IL-10 gene (rs 1800872) was found to be associated with severe varicella ($P = 0.04$) and herpes zoster ($P = 0.01$) in adults. In chickenpox patients, the TT genotype was associated with the development of hepatitis ($\chi^2 = 6.17$, $P = 0.01$). In patients with herpes zoster, the TT genotype had an impact on the development of neurological ($P = 0.03$) and ophthalmic complications ($P = 0.0001$). Secondary bacterial complications were associated with the TG genotype of the IL-10 gene (rs 1800872) carrier state in all the patients ($P < 0.05$). It was proved that TT genotype was associated with an increase in serum IL-10 concentration (rs 1800872) in all the patients with infections caused by varicella-zoster virus on admission. In the course of the disease, the quantitative content of IL-10 decreased in all patients with the TT genotype, but remained elevated at the time of discharge ($P < 0.05$). In patients with chickenpox, the TG genotype carriage caused only an increasing trend in the serum IL-10 concentration not different from that in healthy individuals ($P < 0.05$). At the same time, in patients with herpes zoster, the TG genotype of the IL-10 gene (rs 1800872) was associated with an increased cytokine content both on admission and in the disease dynamics ($P < 0.05$).

Conclusions. Changes in the serum concentration of IL-10 in patients with infections caused by varicella-zoster virus depend on the polymorphism of the IL-10 gene (rs 1800872) that encodes it, and are associated with certain clinical features of chickenpox and herpes zoster.

Ключові слова: вітряна віспа, оперізувальний герпес, інтерлейкін-10, поліморфізм гена.

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Роль інтерлейкіну-10 і вплив поліморфізму гена, що його кодує, на перебіг інфекцій, які викликані вірусом varicella-zoster

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Мета роботи – з'ясувати роль змін кількісного вмісту ІЛ-10 у взаємозв'язку з поліморфізмом гена, що його кодує (rs 1800872), в перебігу вітряної віспи та оперізувального герпесу.

Матеріали та методи. У дослідження залучили 50 дорослих хворих на вітряну віспу та 50 хворих на оперізувальний герпес. Здійснили аналіз кількісного вмісту ІЛ-10 у сироватці крові залежно від генетичного поліморфізму цього цитокіну (rs 1800872) та визначили вплив на перебіг захворювань. Кількісний вміст ІЛ-10 у сироватці крові визначали методом імуноферментного аналізу, визначення однонуклеотидного поліморфізму ІЛ-10 (rs 1800872) в цільній венозній крові пацієнтів виконали методом полімеразної ланцюгової реакції в режимі реального часу. Контрольну групу становили 40 здорових осіб. Статистичне опрацювання даних виконали, використовуючи сформовану базу даних пацієнтів у програмі Statistica for Windows 13 (StatSoft Inc., № JPZ804I382130ARCN10-J).

Результати. Встановили, що ТТ-генотип гена ІЛ-10 (rs 1800872) асоціювався з тяжким перебігом вітряної віспи ($p = 0,04$) та оперізувального герпесу ($p = 0,01$) у дорослих. У хворих на вітряну віспу ТТ-генотип асоціювався з розвитком гепатиту ($\chi^2 = 6,17$, $p = 0,01$). У хворих на оперізувальний герпес ТТ-генотип мав вплив на розвиток неврологічних ($p = 0,03$) та офтальмологічних ($p = 0,0001$) ускладнень. Ускладнення, що зумовлені приєднанням вторинної бактеріальної інфекції, в усіх пацієнтів асоціювалися з носійством TG-генотипу гена ІЛ-10 (rs 1800872) ($p < 0,05$). Доведено, що ТТ-генотип у всіх хворих на інфекції, що викликані вірусом varicella-zoster, асоціювався з підвищенням концентрації ІЛ-10 (rs 1800872) у сироватці крові під час госпіталізації. В динаміці захворювання в усіх хворих із носійством ТТ-генотипу кількісний вміст ІЛ-10 знижувався, але залишався підвищеним на момент виписування ($p < 0,05$). У пацієнтів із вітряною віспою носійство TG-генотипу зумовлювало тільки тенденцію до підвищення концентрації ІЛ-10 у сироватці крові, не відрізняючись від кількісного вмісту цитокіну в сироватці крові здорових осіб ($p > 0,05$). У хворих на оперізувальний герпес TG-генотип гена ІЛ-10 (rs 1800872) асоціювався з підвищеним вмістом цитокіну як під час госпіталізації, так і в динаміці захворювання ($p < 0,05$).

Висновки. Зміни концентрації ІЛ-10 у сироватці крові хворих на інфекції, що викликані вірусом varicella-zoster, залежать від поліморфізму гена ІЛ-10 (rs 1800872), що його кодує, та асоціюються з певними особливостями перебігу вітряної віспи та оперізувального герпесу.

Роль интерлейкина-10 и влияние полиморфизма гена, который его кодирует, в течении инфекций, вызванных вирусом varicella-zoster

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Ключевые слова: ветряная оспа, опоясывающий герпес, интерлейкин-10, полиморфизм гена.

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Цель работы – определить роль изменений количественного содержания ИЛ-10 во взаимосвязи с полиморфизмом гена, который его кодирует (rs 1800872), в течении ветряной оспы и опоясывающего герпеса.

Материалы и методы. В исследование включены 50 взрослых больных ветряной оспой и 50 больных опоясывающим герпесом. Проведен анализ количественного содержания ИЛ-10 в сыворотке крови в зависимости от генетического полиморфизма этого цитокина (rs 1800872) и изучено влияние на течение заболеваний. Количественное содержание ИЛ-10 в сыворотке крови определяли методом иммуноферментного анализа, определение однонуклеотидного полиморфизма ИЛ-10 (rs 1800872) в цельной венозной крови пациентов проводили методом полимеразной цепной реакции в режиме реального времени. Контрольную группу составили 40 здоровых лиц. Статистическую обработку данных осуществляли с использованием сложившейся базы данных пациентов в программе Statistica for Windows 13 (StatSoft Inc., № JPZ804I382130ARCN10-J).

Результаты. Установлено, что TT-генотип гена ИЛ-10 (rs 1800872) ассоциировался с тяжелым течением ветряной оспы ($p = 0,04$) и опоясывающего герпеса ($p = 0,01$) у взрослых. У больных ветряной оспой TT-генотип ассоциировался с развитием гепатита ($\chi^2 = 6,17$, $p = 0,01$). У больных опоясывающим герпесом TT-генотип имел влияние на развитие неврологических ($p = 0,03$) и офтальмологических ($p = 0,0001$) осложнений. Осложнения, обусловленные присоединением вторичной бактериальной инфекции, у всех пациентов ассоциировались с носительством TG-генотипа гена ИЛ-10 (rs 1800872) ($p < 0,05$). Доказано, что TT-генотип у всех больных инфекциями, вызванными вирусом varicella-zoster, ассоциировался с повышением концентрации ИЛ-10 (rs 1800872) в сыворотке крови при госпитализации. В динамике заболевания у всех больных с носительством TT-генотипа количественное содержание ИЛ-10 снижалось, однако оставалось повышенным на момент выписки ($p < 0,05$). У пациентов с ветряной оспой носительство TG-генотипа обусловливало лишь тенденцию к повышению концентрации ИЛ-10 в сыворотке крови, не отличаясь от количественного содержания цитокина в сыворотке крови здоровых лиц ($p < 0,05$). У больных опоясывающим герпесом TG-генотип гена ИЛ-10 (rs 1800872) ассоциировался с повышенным содержанием цитокина как при поступлении, так и в динамике заболевания ($p < 0,05$).

Выводы. Изменения концентрации ИЛ-10 в сыворотке крови больных инфекциями, вызванными вирусом varicella-zoster, зависят от полиморфизма гена ИЛ-10 (rs 1800872), который его кодирует, и ассоциируются с определенными особенностями течения ветряной оспы и опоясывающего герпеса.

Chickenpox, as a primary infection caused by varicella-zoster virus, and herpes zoster, as a result of latent virus reactivation in the body, are topical issues at the present time. About 80–90 million of annual chickenpox cases are recorded in the world [1]. Approximately 4.2 million patients are ill with severe complicated course and hospitalized, in 4200 cases – with a fatal course of the disease [2]. The level of morbidity and economic damage caused by varicella-zoster virus is inferior to only unspecified acute respiratory viral and intestinal infections [3,4].

The high level of chickenpox contagiousness with a significant spread determines almost 100 % probability of disease manifestation in contact persons [5]. Traditional conceptions of chickenpox as a typical childhood infection with mild course of the disease and complete recovery are doubtful due to the studies of many authors [6]. In recent years, there has been an increase in the chickenpox incidence in adults, especially young people, with the highest rates among urban residents [5,6]. The risk of complications and deaths in adults is 25 times higher than in children, the death rate from pneumonia reaches 10 % [4,5]. Among adult patients with chickenpox from 20 years and older, encephalitis develops in 11.6 % of patients, with a fatal outcome – in 27.6 % of patients [7]. The risk of developing complications in chickenpox reaches about 30 %, in people with immunosuppressive state – up to 50 % [8].

The risk of herpes zoster development during the life among population is about 30 %, with a sharp increase in people over 50 years of age. Every year in Europe and the United States, there are 4–5 new cases of shingles per 1.000 population [9]. In Ukraine, the incidence is 12–15 cases per 100.000 population. The recurrence rate of the disease is 14 cases per 1.000 population [10]. The mortality from herpes zoster globally ranges from 0.017 to 0.465 cases per 100.000 population every year [9,10].

It is believed that any complications of the diseases caused by varicella-zoster virus are associated with an insufficient immunological response due to immunodeficiency of various genesis. Previously, it was believed that severe course of the diseases, caused by varicella-zoster virus, develops in individuals with immunodeficiency [11]. However, recently, seriously complicated cases of the diseases in immunocompetent patients have become more frequent. A key link in the pathogenesis of the diseases caused by varicella-zoster virus is cellular immunity, the failure of which leads to increased viral load and as a consequence to dissemination and generalization of the infection. Cytokines and their concentration in the blood of patients have an important role to play in immunopathogenesis of chickenpox and herpes zoster [12]. Modern studies by many scientists have shown the dependence of the immune system reactivity and immune response quality on the single-nucleotide polymorphism of the genes encoding cytokines. The study of cytokine genes and their level in the blood is important in predicting the severity of the disease course, possible complications development, and for a personalized therapy [13]. In our opinion, the study of genetic polymorphism of IL-10 in infectology attracts particular attention [14]. The genetic polymorphism of IL-10 (C819T and G1082A alleles) determination in chronic hepatitis C allowed assessing the effectiveness of therapy and predicting the possible development of liver fibrosis and cirrhosis [15]. In patients with influenza A/H1N1, determination of IL-10 alleles carriage allowed to detect a predisposition to development of pneumonia and predict severe course of the disease [16]. An attempt was made to determine the role of IL-10 gene

polymorphism in resistance to the most common herpesviruses [17]. However, isolated studies have been focused on the genetic polymorphism of interleukins and their quantitative content in infections cased by varicella-zoster virus [18], and immunopathogenesis of severe course and complications development in immunocompetent individuals has not been sufficiently studied, which has predetermined the direction of our study.

Aim

The aim of the work is to find out the role of changes in the quantitative content of IL-10 in association with the polymorphism of gene encoding it (rs 1800872) in the course of chickenpox and herpes zoster.

Materials and methods

The study included 50 patients with chickenpox and 50 patients with herpes zoster, who were treated in the Department No 1 of the Municipal Institution "Zaporizhzhia Regional Infectious Clinical Hospital" of the Zaporizhzhia Regional Council. Among the hospitalized patients with chickenpox, men were 34 (68.0 %), women – 16 (32.0 %), aged 18–49 years old, an average of 20.0 [20.0; 21.0] years. Among patients with herpes zoster, men were 19 (38.0 %), women – 31 (62.0 %). The age of the patients varied from 27 to 85 years and averaging 66.5 [55.0; 77,0] years. All patients underwent traditional laboratory and instrumental examinations on the basis of hospital clinical laboratory. In the presence of clinical evidence, a lumbar puncture was performed with a corresponding examination of cerebrospinal fluid. Magnetic resonance imaging was performed to confirm encephalitis. All the patients with herpes zoster were screened for detection of human immunodeficiency virus antibodies in the blood and had negative results. All patients were included in the study randomly based on an informed consent obtained.

Quantitative serum levels of IL-10 were determined using enzyme-linked immunoassay with a high sensitivity human IL-10 assay (Invitrogen BMS213HS, Austria) and enzyme immunoassay analyzer Sirio-S (SEAC, Italy). The single-nucleotide polymorphism (rs1800872) of the IL-10 gene determination was performed in samples of whole venous blood with a CFX96TM (Bio-Rad Laboratories, Inc., USA) amplifier by real-time polymerase chain reaction with NP-512-100 kits (RF). Depending on the IL-10 gene polymorphism (rs1800872) among patients with chickenpox, 2 groups were formed: 37 patients with the TT genotype and 13 patients with the TG genotype. Patients with herpes zoster were distributed as follows: 30 patients with the TT genotype and 20 patients with the TG genotype. Special studies were performed at the Medical Training and Laboratory Center of Zaporizhzhia State Medical University (headed by A. V. Abramov, MD, PhD, DSc, Professor). The control group consisted of 40 healthy persons, aged 21–87 years, with an average age of 28.0 [22.0, 55.0] years. Among healthy individuals, the TT genotype was registered in 14 persons, the IL-10 (rs 1800872) TG genotype – in 26 patients. Quantitative serum content of IL-10 in healthy individuals did not depend ($P > 0.05$) on the IL-10 (rs 1800872) gene polymorphism.

Statistical data was analyzed using the current patient database in Statistica for Windows (version 13; StatSoft Inc., No JPZ804I382130ARCN10-J). The χ^2 method was used to analyze the genotypes distribution between the study groups. The odds ratio (OR) was calculated according to the formula: OR = ad/bc, where a is the frequency of a particular allele in the group of patients with varicella-zoster virus cased infections, b is the frequency of a particular allele in the comparison group, c and d are the total frequency of other alleles in the study and comparison group, respectively. The 95 % confidence interval (CI) for OR was calculated using the Woolf method [19]. To assess the significance of differences between the quantitative features in the independent groups, the Mann-Whitney criterion was used, and in the dependent groups, the Wilcoxon criterion was used. The relationship between the studied parameters was determined using the Kendal Tau τ rank correlation method. Statistically significant differences were considered at $P < 0,05$.

Results

As a results of the study, it was found that the TT genotype, unlike the TG genotype of IL-10 (rs 1800872) gene, in patients with varicella-zoster virus caused infections was associated with severe course of chickenpox (100 % vs. absence, $\chi^2 = 4.39$, $P = 0.04$) and herpes zoster (86.7 % vs. 13.3 %, $\chi^2 = 6.35$, $P = 0.01$) (*Table 1*). The additive inheritance model served to confirm the association between the IL-10 (rs 1800872) TT genotype presence and high risk of developing severe course of chickenpox (1.000 vs. 0,000, $\chi^2 = 4.39$, OR = 10.31 95 % CI = 0.56–189.41) and herpes zoster (0.867 vs. 0.133, $\chi^2 = 6.35$, OR = 6.88 95 % CI = 1.35–35.11).

The analysis of the developed complications spectrum in patients showed the influence of the IL-10 (rs 1800872) polymorphism on the risk of certain types of complications development in patients with different clinical forms of infection caused by varicella-zoster virus. Thus, in patients with chickenpox, the TT genotype, unlike the TG genotype, was associated with visceral complications development (100 % vs. absent, $\chi^2 = 9.05$, $P = 0,003$), mainly hepatitis (100 % vs. absent, $\chi^2 = 6.17$, $P = 0.01$). In patients with herpes zoster, the TT genotype was not associated with visceral complications development ($P > 0.05$), but it had statistically significant relationship with the development of neurological (85.7 % vs. 14.3 %, $\chi^2 = 4.75$, $P = 0.03$) and ophthalmic complications (76.2 % vs. 23.8 %, $\chi^2 = 14.75$, $P = 0.0001$) (*Table 1*).

Analyzing the spectrum of complications in patients with infections caused by varicella-zoster virus, attention has been drawn to clear association between development of complications due to secondary bacterial infection and the TG genotype in patients with chickenpox (87.5 % vs. 12.5 %, $\chi^2 = 18.72$, $P = 2.0E-5$) and herpes zoster (80.0 % vs. 20.0 %, $\chi^2 = 8.33$, $P = 0.004$) (*Table 1*).

The TT genotype presence in patients with infections caused by varicella-zoster virus was accompanied by a more significant increase in the serum quantitative content of IL-10, unlike the TG genotype carriers. In acute period of chickenpox, this figure was the highest in patients with the TT genotype and 16.4 times ($P = 0.000076$) exceeded

the serum concentration of IL-10 in the TG genotype carriers. In the disease dynamics, the TT genotype carriers showed decreased level of IL-10 (P = 0.000099), however, this parameter remained higher than in healthy subjects (P < 0.05) at the time of hospital discharge. It should be noted that in the TG genotype carriers with chickenpox, the IL-10 serum content only tended to increase during the whole period of observation and didn't statistically differ from the index in healthy individuals (P > 0.05) (*Table 2*).

Similar patterns of the IL-10 serum content dynamics depending on the polymorphism of the gene encoding it were also established in patients with herpes zoster, but these changes had certain peculiarities. The IL-10 serum content was the highest in the TT genotype carriers on admission and 4.8 times (P = 0.03) exceeded the similar index in the TG genotype carriers. However, it should be noted that in patients with herpes zoster, unlike patients with chickenpox, in the TG genotype presence, the serum content of IL-10 was higher than in healthy subjects (P < 0.05) on admission. In the dynamics, the serum content of IL-10 decreased but remained higher at the time of discharge than in healthy subjects, as in the TT genotype carriers (P < 0.05) and in the TG genotype of the IL-10 (rs 1800872) gene polymorphism (P < 0.05) presence (*Table 3*).

The Kendal Tau correlations between the quantitative serum content of IL-10 and hemogram parameters were established to demonstrate the role of this cytokine changes in the course of diseases caused by varicella-zoster virus. Thus, in patients with chickenpox, the serum content of IL-10 had an inverse correlation with a quantitative level of blood leukocytes (τ = -0.29, P = 0.008) and band neutrophils percentage (τ = -0.23, P = 0. 04) as well as a direct correlation with the blood eosinophils percentage (τ = +0.29, P = 0.01), which confirms the correlation between low content of this cytokine and formation of complications associated with secondary bacterial infection and the severity of intoxication syndrome. In patients with herpes zoster, the serum content of IL-10 also had an inverse correlation with the white blood cells count (τ = -0.22, P = 0.04).

Table 1. Characteristics of the course of infections caused by varicella-zoster virus depending on the IL-10 gene (rs 1800872) polymorphism, abs. (%)

Patients with chickenpox (n = 50)		
Indicator	**TT genotype (n = 37)**	**TG genotype (n = 13)**
Course of the disease:		
– severe (n = 10)	10 (100 %)*	0 (0 %)
– moderate (n = 40)	27 (72.5 %)	13 (27.5 %)
Development of complications:		
– complicated (n = 33)	25 (75.7 %)	8 (24.3 %)
– uncomplicated (n = 17)	12 (70.6 %)	5 (29.4 %)
Visceral complications (n = 17)	17 (100 %) *	0 (0 %)
Hepatitis (n = 13)	13 (100 %) *	0 (0 %)
Pneumonia (n = 4)	4 (100 %)	0 (0 %)
Neurological complications (n = 2)	2 (100 %)	0 (0 %)
Ophthalmic complications (n = 7)	5 (71.4 %)	2 (28.6 %)
Secondary bacterial infection (n = 8)	1 (12.5 %)*	7 (87.5 %)
Patients with herpes zoster (n = 50)		
Indicator	**TT genotype (n = 30)**	**TG genotype (n = 20)**
Course of the disease:		
– severe (n = 15)	13 (86.7 %)*	2 (13.3 %)
– moderate (n = 35)	17 (48.6 %)	18 (51.4 %)
Development of complications:		
– complicated (n = 37)	19 (51.3 %)	18 (48.7 %)
– uncomplicated (n = 13)	7 (53.8 %)	6 (46.2 %)
Hepatitis (n = 10)	6 (60.0 %)	4 (40.0 %)
Neurological complications (n = 7)	6 (85.7 %) *	1 (14.3 %)
Ophthalmic complications (n = 21)	16 (76.2 %) *	5 (23.8 %)
Secondary bacterial infection (n = 10)	2 (20.0 %) *	8 (80.0 %)
Postherpetic neuralgia (n = 3)	3 (100 %)	0 (0 %)

***:** the difference is significant compared with the TG genotype carriers (P < 0.05).

Table 2. Dynamics of the quantitative serum content of IL-10 in patients with chickenpox depending on the IL-10 (rs 1800872) gene polymorphism, Me [Q_{25}; Q_{75}] pg/ml

Period of observation	**Health people (n = 40)**	**Patients with chickenpox (n=50)**	
		TT genotype (n = 37)	**TG genotype (n = 13)**
On admission	0.56 [0.37; 0.75]	14.08 [2.66; 38.76] [1]	0,86 [0,57; 1,48] [2]
At discharge		1.20 [0.72; 1.88] [1,3]	0,72 [0,52; 0,88] [2]

1: the difference is significant compared to healthy people (P < 0.05); **2:** to patients with the TT genotype in the corresponding period of observation (P < 0.05); **3:** to patients with the corresponding genotype on admission (P < 0.05).

Table 3. Dynamics of the quantitative serum content of IL-10 in patients with herpes zoster depending on the IL-10 (rs 1800872) gene polymorphism, Me [Q_{25}; Q_{75}] pg/ml

Period of observation	**Health people (n = 40)**	**Patients with herpes zoster (n=50)**	
		TT genotype (n = 30)	**TG genotype (n = 20)**
On admission	0.56 [0.37; 0.75]	6.92 [3.1; 10.88] [1]	1.44 [0.80; 5.02] [1,2]
At discharge		0.82[0.66; 2.02] [1,3]	1.05[0.52; 1.12] [1]

1: the difference is significant compared to healthy people (P < 0.05); **2:** to patients with the TT genotype in the corresponding period of observation (P < 0.05); **3:** to patients with the corresponding genotype on admission (P < 0.05).

Discussion

Infections caused by varicella-zoster virus are quite common diseases with the presence of various clinical forms, development of severe complications and possible recurrence of the disease after endogenous virus reactivation. Th1-type cellular immunity including cytokines and their immunoregulatory functions have an essential role to play in controlling varicella-zoster virus disintegration and generalization. The production of cytokines by innate and acquired immune cells is an important link in the immune defense against varicella-zoster virus [11,20]. It is known that IL-10 is a major anti-inflammatory cytokine that limits inflammatory processes, inhibits pro-inflammatory reactions preventing tissue damage. However, viruses have eveloped resistance that exploits the immunoregulatory function of IL-10 to suppress immunity promoting their own survival [14,21]. It has been found that IL-10 is important for limiting tissues damage during acute phase of immune responses and can be synthesized by many immune cells as well as mediate the function of these cells. Currently, regulatory mechanisms of IL-10 are actively studied, which influence the quality of antiviral immune response and chronization of infectious diseases [22]. In particular, it has been shown that an increase IL-10 levels is important for inducing immunity in varicella-zoster virus infections, which ultimately affects the recurrence rate and the disease severity [11,23]. With the appearance of molecular genetic studies, that allowed the genetic polymorphism of interleukins detection, there was an opportunity to deepen the ideas about chickenpox and herpes zoster immunopathogenesis. According to our

study, it has been shown that in patients with chickenpox, the TT genotype of IL-10 (rs 1800872) gene polymorphism was associated with the severe course (1.000 versus 0.000, χ^2 = 4.39, OR = 10.31, 95 % CI = 0.56–189.41), visceral complications development (P < 0.005) and higher serum concentration of cytokine in patients (P = 0.000076). Works focused on the study of the IL-10 gene polymorphism in patients with chickenpox were not found in the literature available, and the cytokine status study in patients with chickenpox was predominantly conducted among children. Thus, in children with the moderate disease duration, there was an increase in IL-1β, moderate elevation of IL-10, decrease in IL-2 at the normal levels of IL-6 and IL-4. In severe forms, on the contrary, insufficient immunological reactivity of the organism, characterized by unchanged levels of IL-1β, IL-10 and IL-4 with significantly decreased IL-6, was noted [24]. Some scientists point out that the more severe course of chickenpox in adults is due to differences in immune response in children and adults. In immune system of children, unlike adults, phagocytes predominate, being a link of cellular immunity and major in the immunological defense of the organism against varicella-zoster virus [25]. Our study found that in patients with herpes zoster, the TT genotype had an association with severe course and development of neurological (P < 0.05) and ophthalmic (p <0,0005)complications as well as with higher serum levels of IL-10 (P = 0.03). The results of our study are to some extent linked to the results of other researchers [26], which have proven the special role of the IL-10 ATA haplotype, the presence of which had caused the reactivation of this virus. According to another study [27], the increased risk of herpes zoster is associated with the GCC polymorphism carrier of the IL-10 (1082 allele). In determining the quantitative content of IL-10 in patients with herpes zoster, some authors [23,26] found that an increased level of cytokine in blood causes an adequate immune system response and leads to a moderate course of the disease. An inadequate immunoreactivity of the organism and a constant blood level of the cytokine characterized the severe course of herpes zoster in patients. However, other scientists have found that immune complex-mediated sharp increase in IL-10 production by macrophages results in a decrease in specific antiviral immunity leading to the infection generalization and chronicity [28].

There are limited studies in the current scientific literature with regard to the evaluation of cytokines role in bacterial complications development in patients with chickenpox and herpes zoster. So, the study [11] has shown that the values of IL-6 and interferon-ɣ may be associated with a high risk of developing bacterial skin complications. Our study determined the role of the TG genotype of the IL-10 (rs 1800872) gene polymorphism carriage as a high risk for developing complications associated with secondary bacterial infections in patients with herpes zoster (P = 0.004) and chickenpox (P = 2.0E-5) that was accompanied either by the absence of changes (P > 0.05) or insignificant increase (P < 0.05) in the serum IL-10 content as compared to healthy people.

Conclusions

1. Changes in the serum levels of IL-10 in patients with infections caused by varicella-zoster virus depend on the gene polymorphism (rs 1800872) encoding it, and are associated with certain clinical features of chickenpox and herpes zoster.

2. In TT genotype carriers with chickenpox, the serum IL-10 content is 16.4 times (P = 0.000076) higher than that in TG genotype carriers in the acute period of the disease. In addition, in patients with chickenpox, the TT genotype, unlike the TG genotype of the IL-10 (rs 1800872) gene polymorphism, is associated with severe course (1,000 versus 0.000, χ^2 = 4.39, OR = 10.31 95 % CI = 0.56–189.41) and development of visceral complications (P < 0.005).

3. In patients with herpes zoster and the TT genotype presence, the serum content of IL-10 is 4.8 times higher than that in TG genotype carriers (P = 0.03). In patients with herpes zoster, the TT genotype has association with the severe course (0.867 vs. 0.133, χ^2 = 6.35, OR = 6.88 95 % CI = 1.35–35.11) and development of neurological (P < 0.05) and ophthalmic (P < 0.0005) complications.

4. In infections caused by varicella-zoster virus, the development of complications associated with secondary bacterial infection is accompanied either by the absence of changes (P > 0.05) or the slight increase (P < 0.05) in the serum content of IL-10 compared with healthy people, and is clearly associated with the TG genotype (80.0 % vs. 20.0 %, P < 0.005).

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