

IMMEDIATE RESULTS OF COMPLEX TREATMENT OF CHILDREN WITH CHRONIC TONSILLITIS AND CHRONIC ADENOIDITIS ASSOCIATED WITH CMV AND EBV.

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Annotation. Most researchers have concluded that cytomegalovirus infection may contribute to the exacerbation of many chronic and recurrent diseases. In addition, they can cause direct, autoimmune reactions in the body [2,4,5].

Gossman W. G et al [2018] defined several forms of cytomegalovirus infection in the organism depending on the course of the infection: primary infection if no cytomegalovirus has been previously identified in a person, re-infection or reactivation if CMVI has been previously identified in the organism; the course can be acute, latent or chronic in congenital or acquired CMVI [6,7,8,9].

In acute CMV infection, all tissues are affected. Nigro G. et al [2015] found that cytomegalovirus infection, if T-cell immunity is reduced in the organism, can invade the body for a long time and then the infection can manifest itself as a subacute course [10,11].

Jones R. P. et al [2014] and Kallemeijn M. J. [2017]. et al in their studies found that children with congenital cytomegalovirus infection have a very high incidence of death, neurological impairment and in addition HIV infection progresses faster in them [1,3,7].

Purpose of the study. To evaluate the immediate results of complex treatment of children with chronic tonsillitis and chronic adenoiditis associated with CMVI and VEB. Материалы и методы исследования.

Clinical observation was carried out in 116 patients with chronic tonsillitis (simple form) and adenoiditis associated with VEB and cytomegalovirus, aged from 4 to 14 years, as well as 66 patients with tonsillitis (simple form) and adenoiditis in the comparison group. The control group of 30 patients of similar age was carried out inpatient and outpatient on the basis of the multidisciplinary clinic of SamSMU in the department of otorhinolaryngology, children's department and consultative polyclinic. In addition to general clinical and standard methods of examination of chronic tonsillitis and adenoiditis, in order to determine the state of humoral immunity to CMV infection, serological examination by enzyme-linked immunosorbent assay (ELISA) with the determination of species-specific IgM and IgG was performed. Species-specific antibodies of IgG class to CMV were determined by ELISA using a reagent kit "CMV IgG Immulite 2000 Systems" on an automatic analyser Immulite 2000 (Siemens, USA).

IgG class antibodies were evaluated by ELISA results using an index of optical density automatically calculated by the device. If the OD index value is less than 0.8 - negative result, indicating the absence of species-specific antibodies of IgG class; more than 1.1 - positive result; AI index values in the range of 0.9-1.0 were considered as a doubtful result. IgM class antibodies and IgG avidity index to CMV were determined by enzyme-linked immunosorbent assay using VectoCMV-IgM and VectoCMV-IgG-avidity reagents (VectorBest, Russia). IgG avidity was determined only in children whose serum showed antibodies to CMV class IgG. Children with IgM-class CMV antibodies were considered as acute infectious process and were

not included in the study and referred to an infectious disease specialist.

To confirm the presence of CMV in biological material, molecular biological research methods were used - detection of CMV DNA in biological material. The amount of CMV DNA was determined in whole blood of the examined subjects by PCR with hybridisation-fluorescence detection of CMV in real-time mode (Real-time) on the analyser IQ-5Cycler ("BioRad", CIA) using the reagent kit "AmpliSense®CMV-screen/monitor-FL". Analytical characteristic of the test system used: sensitivity - 400 copies/ml; linear measurement range of the reagent kit - 400-10000000 copies/ml. If the result is greater than 10000 000, it is given as a result of more than 10 000 000 copies/ml. If the result is less than 400 copies/ml, it is reported as less than 400 copies/ml. The specific sensitivity of the reagent kit is shown by examining the reference strain AD169.

DNA of human herpes virus type 4 (HEV) was determined in peripheral blood samples by PCR with real-time hybridisation-fluorescence detection of the analysis results quantitatively using the AmpliSensHAVU Screen FL reagent kit according to the manufacturer's instructions.

In addition to standard methods of treatment in children with chronic tonsillitis and adenoiditis associated with CMVI and VEB, along with traditional therapy the patients were prescribed Groprinosin as antiviral therapy. Children were prescribed a daily dose of 50 mg/kg of body weight in 3-4 doses for 5-7 days, then, after a 5-day break the patients were prescribed a repeated course of Groprinosin according to the above scheme. The effectiveness of therapy was evaluated in dynamics by clinical signs, laboratory parameters during the exacerbation of the disease was carried out once every six months for one year.

Results and their discussion. To evaluate the effectiveness of complex treatment, we carried out catamnestic observations. They were carried out within a year after the treatment. Catamnestic observations were carried out in 111 children, aged from 4 to 14 years. At the catamnestic observation of indicators of humoral immunity in children with HT associated CMVI and VEB are presented in Table 1.

Table 1.

Indices of humoral immunity in children with chronic tonsillitis associated with CMVI and VEB (1 year after treatment)

Age	IgM		IgG		Ig A		Ig E	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
4-6 age	4.56 ± 0.14*	2.56 ± 0.13*	14.3 ± 1.14	12.1±1.43	1.3 ±0.04*	1.3 ±0.04*	45,0±1.52*	45,0±1.52*
7-10 age	2.65 ± 0.18*	2.55 ± 0.18*	12.6 ± 1.01	11.7±0.78	0.67 ± 0.09*	0.67 ± 0.09*	58.6 ±2.06*	33.5±1.20*
11-14 age	4.7±0.05*	2.7±0.05*	6.7 ±0.15*	13,5±1.23*	0.95±0.2*	0.95±0.2*	34.0 ±1.18	34.0 ±1.18
References	1,5± 0,14		10,2± 0,63		1,1 ±0,2		32,6 ±3,23	

* -p<0.05 reliability of indicators between the examined children and the control group.

The analysis showed that after 1 year of complex treatment the IgM content in all age groups in children with chronic tonsillitis associated with CMVI and VEB decreased. (2.56 ± 0.13 ; 2.55 ± 0.1 ; 2.7 ± 0.05 , respectively) IgG in the age groups 4-6 years and 7-10 years also decreased compared to the pre-treatment values (see Table 4.10), and at the age of 11-14 years it significantly approached the norm. For IgA, there was a trend towards normalisation in all age categories. IgE has decreased significantly, but still some increase in the amount of its content is still present.

We also analysed the indices of humoral immunity in children with chronic adenoiditis associated with CMVI and VEB one year after treatment.

Table 2 shows the data of children with chronic adenoiditis associated with CMVI and VEB depending on the level of adenoid tissue enlargement and the age of the child. At level I of adenoid tissue enlargement in children from 4 to 6 years of age, there was an increase in IgM (1.87 ± 0.21), IgG (11.9 ± 1.08) and IgE (25.6 ± 3.24), the amount of IgA (0.85 ± 1.2) was normalised.

Table 2

Indices of humoral immunity in children with chronic adenoiditis associated with CMVI and VEB (4-6 years old) (1 year after treatment)

Degree of adenoid tissue enlargement	IgM		IgG		IgA		IgE	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
I	$1,88 \pm 0,21^*$	$1,87 \pm 0,21^*$	$9,25 \pm 1,12^*$	$11,9 \pm 1,08^*$	$0,85 \pm 1,2$	$0,85 \pm 1,2$	$78,6 \pm 5,54^*$	$25,6 \pm 3,24^*$
II	$1,54 \pm 0,01$	$1,52 \pm 0,01$	$7,85 \pm 0,54$	$13,01 \pm 1,45$	$0,52 \pm 0,015^*$	$0,74 \pm 0,02^*$	$112,5 \pm 15,54^*$	$55,9 \pm 4,17^*$
III	$1,87 \pm 0,2^*$	$1,86 \pm 0,2^*$	$9,02 \pm 0,5$	$10,22 \pm 0,29$	$0,35 \pm 0,08^*$	$0,65 \pm 0,08^*$	$140,5 \pm 12,5^*$	$25,4 \pm 3,27^*$
References	$0,87 \pm 0,05$		$8,18 \pm 0,22$		$0,8 \pm 0,05$		$24,4 \pm 4,8$	

* -p<0.05 reliability of indicators between control and studied groups.

The analysis of the indicators of humoral immunity II level of adenoid tissue enlargement in children aged 7 to 10 years showed the content of IgM (1.15 ± 0.17), IgG (11.71 ± 0.89) and IgE (55.9 ± 4.17), the amount of IgA (0.74 ± 0.02) within the normal range. Compared to pre-treatment much the indices normalised, except for IgE, which decreased much but still remained significantly above normal.

Table 3 also presents the analysis of the indicators of humoral immunity III level of adenoid tissue enlargement in children aged 7 to 10 years showed also normalisation or approaching of the indicators to the reference values. IgM(1.75 ± 0.04), IgG (12.24 ± 4.54) and IgE (33.25 ± 3.63), the amount of IgA (0.88 ± 0.03) within the normal range.

Table 3.

Indices of humoral immunity in children with chronic adenoiditis associated with CMVI and VEB (7-10 years old) (1 year after treatment)

Enlargement of adenoid tissue	IgM		IgG		IgA		IgE	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
I	1.44 ± 0.04	1.15 ± 0.17	6.25 ± 0.05	12.32 ± 1.06	$0.62 \pm 0.3^*$	$0.62 \pm 0.3^*$	$56.0 \pm 2.49^*$	$36.0 \pm 1.85^*$
II	$1.99 \pm 0.25^*$	$1.99 \pm 0.25^*$	8.22 ± 0.07	11.71 ± 0.89	$0.74 \pm 0.02^*$	$0.74 \pm 0.02^*$	$75.7 \pm 7.49^*$	$55.9 \pm 4.17^*$
III	$1.75 \pm 0.04^*$	$1.75 \pm 0.04^*$	$15.87 \pm 3.44^*$	$12.24 \pm 4.54^*$	$0.87 \pm 0.03^*$	$0.88 \pm 0.03^*$	85.9 ± 5.11	33.25 ± 3.63
References	$1,5 \pm 0,14$		$10,2 \pm 0,63$		$1,1 \pm 0,2$		$32,5 \pm 3,21$	

* - $p < 0.05$ reliability of indicators between control and studied groups.

In catamnesis in children aged 11-14 years at all levels of adenoid tissue enlargement compared to the indicators before treatment much improved, especially the content of IgG and IgE. The data are presented in Table 4.

Table 4.

Indices of humoral immunity in children with chronic adenoiditis associated with CMVI and VEB (11-14 years old) (in catamnesis)

Enlargement of adenoid tissue	IgM		IgG		IgA		IgE	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
I	$1.78 \pm 0.09^*$	$1.78 \pm 0.09^*$	8.56 ± 1.09	11.24 ± 2.65	1.12 ± 0.07	1.12 ± 0.07	$98.7 \pm 9^*$	$34.2 \pm 2.39^*$
II	$0.65 \pm 0.13^*$	$1.65 \pm 0.09^*$	10.65 ± 1.13	10.65 ± 1.13	$0.65 \pm 0.12^*$	$0.65 \pm 0.12^*$	$66.2 \pm 13^*$	$28.5 \pm 3.47^*$
III	$0.80 \pm 0.05^*$	$1.87 \pm 0.05^*$	$9.33 \pm 1.56^*$	$12.33 \pm 1.54^*$	$0.83 \pm 0.15^*$	$0.83 \pm 0.15^*$	84.6 ± 5.16	34.6 ± 2.26



норма	1,5± 0,14	10,2± 0, 63	1,1 ±0,2	32,6 ±3,23
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* * - $p < 0.05$ reliability of indicators between control and studied groups.

Conclusions. Thus, interpretation of humoral immunity data showed normalisation of all immunoglobulin classes in chronic tonsillitis one year after treatment, except for IgE, which was still slightly elevated. Children with adenoiditis also showed normalisation of immunoglobulin indices, except for children with level III adenoid tissue enlargement, they also retained an increase in the amount of IgE.

Dynamic observation revealed that in children with adenoiditis the number of exacerbations per year was 6.3 ± 1.02 times, after complex therapy this number decreased to 4.08 ± 0.54 times, in children with adenoiditis with adenoid tissue enlargement of II, III levels exacerbations were slightly more frequent and were 7.7 ± 1.02 ; 7.1 ± 1.01 respectively, after the treatment more rare exacerbations of the disease were also noted and made $4,13 \pm 0,6$; $4,8 \pm 0,54$ respectively.

Thus, complex treatment had a positive effect on the immune status of children with HT and CA, which led to a decrease in the number of exacerbations.

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