

Improving Treatment and Rehabilitation of Children with Hearing Loss Due to Toxoplasmosis and Cytomegalovirus Infection

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Abstract Treatment of sensorineural hearing loss (SNHL) over the last decades remains one of the most urgent problems of modern otorhinolaryngology and serology. Despite certain successes achieved in recent years, the number of people with hearing defects is increasing to a large extent due to this pathology. According to some authors, SNHL on the background of toxoplasma and CMV infection significantly affects the quality of life of children, in addition, the importance of the issues of diagnosis, treatment and rehabilitation of patients with hearing loss is largely determined by the fact that this pathology is among the socially significant and affects all age groups of the pediatric population. Despite the availability of a variety of methods for the treatment of SNHL on the background of toxoplasma and CMV infection, the problem is far from being solved. Drug therapy of sensorineural hearing loss based on the etiological factor and background diseases leads to increased treatment efficacy and improved socialization of children. Therefore, an urgent and reasonable task in the problem of treatment of SNHL is the search for new methods of therapy depending on the etiologic factor of this pathology.

Keywords Cytomegalovirus infection, Toxoplasma infection, Interleukins, Sensorineural hearing loss, Luciferin

1. Introduction

Despite the achievements in the field of otorhinolaryngology to this day sensorineural hearing loss is one of the leading places in the structure of pediatric morbidity. According to WHO data, the incidence of hearing loss in children ranges from 1 to 2% and 0.02% of them are children with sensorineural hearing loss of various degrees. It has been revealed that in early childhood this type of hearing loss occurs in 82% of children, i.e. before the development of speech, it should be noted that, of these children, in the perinatal period, disorders appear in 38.5% of children.

Analysis of foreign and domestic literature has shown that the pathogenesis of hearing loss in children and adults is based on multifactorial causes. Over the last 15 years, the incidence of sensorineural hearing loss in Uzbekistan, especially in young children, has more than doubled. Currently, almost 7% of the population has hearing impairment, with sensorineural disorders accounting for 70-80%. In recent decades, there has been a trend towards an increase in the incidence of SNHL hearing loss in children, with viral

infections being the main cause. Analysis of the literature has shown that researchers have studied the clinical and audiological characteristics of sensorineural hearing loss (SNHL) due to the association of toxoplasma and CMV infection.

The aim of the study is to improve the results of treatment and rehabilitation in children with hearing loss on the background of toxoplasma and cytomegalovirus infection and on this basis to develop a therapeutic and diagnostic algorithm.

2. Materials and Methods

The work was carried out in the period from 2021 to 2023 at the Department of Otorhinolaryngology №2 and in the Consultative Polyclinic of the Multidisciplinary Clinic of Samarkand State Medical University. The object of the study was 115 children in the age category from 1 to 7 years with SNHL in association with toxoplasmosis and CMV, who were included in the main group and in the comparison group of 30 children diagnosed with SNHL without toxoplasmosis and CMV infection. Group I patients received traditional therapy according to the age dosage, in combination of antiviral (Proteflazid) and immunocorrective therapy (Galavit 50 mg

in the form of suppositories according to the scheme). Group II patients received only conventional therapy.

The diagnosis of sensorineural hearing loss was formed (H90.3 Bilateral sensorineural hearing loss) according to WHO requirements and classified according to the international classification of disease ICD-10. Anamnestic, clinical, laboratory, and instrumental examination data of patients were taken into account in making the diagnosis of the disease. All patients were examined by general clinical, clinical-immunologic, and virologic methods. Infection with toxoplasmosis and CMVI pathogens was determined by enzyme-linked immunosorbent assay (ELISA) and polymerase chain reaction (PCR). Endoscopic ear examination, tympanometry, OAE and SHLHP were also performed in all patients. The results of the study of anamnestic data on the causes of hearing loss revealed that the main cause of hearing loss in sick children was an unfavorable course of pregnancy in mothers against the background of toxoplasma and cytomegalovirus infection.

In the course of objective examination the following clinical signs were found in the patients: in the main group all 115 (100%) patients showed signs of anemia, in the comparative group this index was 43.4% (13) respectively, sub febrile temperature in the main group was observed in

61.7% (71) patients, enlarged lymph nodes in the main group were palpated in 91 (79.1%) patients, 50.4% (58) cases were observed lethargy in children of the main group, decreased appetite in both groups was found in 72 (62.6%) and 6 (20%) patients respectively. No enlargement of lymph nodes, sub febrile temperature and lethargy was observed in children in the comparison group in 7 (23.3%) children respectively.

The results obtained on CSVС showed that in the main group I degree of SNHL was registered in 17 (14.8%) patients, in the comparison group in 4 (13.3%) children. II degree of SNHL in 35 (30.4%) in the main group, 10 (33.3%) in children of the comparison group. In 53 (46.1%) children of the main group and in 8 (26.7%) children of the comparison group the III degree of SNHL was registered. IV degree of SNHL was registered in 10 (8.7%) children of the main group and in 8 (26.7%) children of the comparison group. The results of our research showed that in all the studied children in both groups tympanometry revealed type A and the result of OAE was evaluated as "failed".

To confirm the presence of these infections, we performed molecular diagnostics (PCR). In children of the main group DNA of toxoplasma and CMV infection was detected in blood serum and in the comparison group PCR result was negative.

Table 1. Comparative analysis of immune indices in patients with SNHL before treatment

Indicators	Main group (n=115)		Comparative group (n=30)		P
	M	m	M	m	
IL-4 (3-8 pg/ml)	16,31	0,32	5,74	0,26	p<0,001
IL-18 (40- pg/ml)	149,24	3,04	62,13	2,69	p<0,001
LF (650-1000 ng/ml)	1564,66	22,51	810,55	21,18	p<0,001
CRP (general) 0-10 mg/l	16,00	0,16	5,30	0,53	p<0,001
CRP (highly sensitive.) (HsCRP) (0-1 mg/l)	3,69	0,22	0,60	0,05	p<0,001

Note: P- reliability of differences between the main and comparison groups before treatment;

Table 2. Indicators of clinical syndromes before and after treatment in both groups

Clinical signs	Main group (n=115)		Comparative group (n=30)	
	Before treatment	After treatment	Before treatment	After treatment
Grade I anemia	42 (36,5%)	Within normal limits	13(43,3%)	13(43,3%)
Grade II anemia	73(63,5%)	73(63,5%) has changed to grade I anemia	17(56,7%)	17(56,7%)
Subfebrile temperature	71(61,7%)	Within normal limits	-	-
Enlargement of lymph nodes	91(79,1%)	11(9,6%)	-	-
lethargy	58(50,4%)	Within normal limits	7(23,3%)	7(23,3%)
	72(62,6%)	8(7,0%)	6(20,0%)	6(20,0%)
Decreased appetite	115(100%)	Improved by 10 to 15 dB	30(100%)	Unchanged

The results of immunologic examination of children, showed that the characteristic signs before treatment in the main group were found to be increased content of proinflammatory interleukins IL-4, IL-18, as well as lactoferrin, total and high-sensitivity C-reactive protein (table 1).

Based on this, we performed the above conservative treatment in both groups and obtained the following results after treatment.

Study results. According to our results after the complex treatment, clinical signs and associated pathologic phenomena changed in positive dynamics (table 2).

Among the examined 25 (21.7%) children of the main group with SNHL on the background of IV degree toxo- and CMV infection and 8 (26.7%) children of the comparison group with SNHL, in addition to the above-mentioned treatment, hearing implantation was performed. Of these, 6 (5.2%) children of the main group with SNHL on the background of toxo- and CMV infection underwent cochlear implantation (CI) according to the indications. Out of 8 (26.7%) children of the comparison group with the diagnosis of SNHL of IV degree, 3 (37.5%) patients underwent CI and 5 (62.5%) children were included in the state program for cochlear implantation. It should be noted that the results of our complex treatment show normalization of hearing in 7 (10.8%) children.

3. Results and Discussions

After treatment specific antibodies IgM to toxoplasmosis and CMV in the main group significantly decreased to the level of normal 0.26 ± 0.01 and 0.52 ± 0.01 respectively, which shows the cure of acute period of infection ($p < 0.001$). Specific IgG antibodies to toxoplasmosis and CMV in this group after treatment significantly amounted to 0.25 ± 0.00 and 0.048 ± 0.02 respectively, which indicate the beginning of remission ($p < 0.001$). It should be noted that in the comparative group after the treatment there were no tests for specific antibodies to toxoplasmosis and CMV infection, as this group consisted of patients with SNHL without these infections.

In order to solve the set objectives, we also performed post-treatment SHLHP in the studied groups. As the results showed, in group I children with SNHL on the right side was diagnosed in 38.31 ± 1.12 patients, SNHL on the left side in 47.31 ± 1.12 patients. As for the comparative group with SNHL I degree on the right side, it was significantly diagnosed in 28.0 ± 2.83 patients ($p < 0.001$). On the left side, this degree in the comparison group was diagnosed in 37.5 ± 3.54 patients, respectively ($p < 0.001$). SNHL of I-II degree on the right side in the main group was diagnosed in

48.81 ± 0.07 patients, on the left side in 58.3 ± 0.96 patients. The distinctive feature of this index was that in the comparison group, in 39.0 ± 1.12 patients, I-II degree SNHL of the right side was reliably determined in 39.0 ± 1.12 patients ($p < 0.001$), while on the left side it was reliably determined in 50.0 ± 2.50 children ($p < 0.01$). Grade II SNHL on the right side in the main group was determined in 56.52 ± 0.75 children and on the left side in 62.61 ± 0.63 children ($p < 0.001$).

In the comparison group, this degree of SNHL on the right side was significantly diagnosed in 46.25 ± 2.02 children and on the left side in 51.00 ± 2.26 patients, respectively ($p < 0.001$). There was not a strong feature of difference between the main and comparison group in the occurrence of SNHL grade II-III on the right side, which was reliably diagnosed in 62.63 ± 0.82 of the main group and 52.50 ± 1.87 patients of the comparison group respectively and on the left side in 65.53 ± 0.54 and 60.83 ± 0.91 patients respectively by group ($p < 0.001$). In the comparative aspect, in the main group children, SNHL of grade III was diagnosed on the right in 65.45 ± 0.32 and on the left in 72.91 ± 0.54 patients, in the comparison group on the right in 61.25 ± 1.44 and on the left in 68.75 ± 1.44 patients respectively ($p < 0.01$). Prominent improvements in the main group of SNHL grade III-IV on the right side was diagnosed in 76.57 ± 1.00 children and on the left side in 96.29 ± 0.70 children respectively ($p < 0.05$). The main tendencies in hearing improvement were observed in the main group, which received complex therapy, as the IV degree SNHL on the right side was diagnosed in 94.00 ± 1.41 children ($p < 0.001$) and on the left side in 96.00 ± 1.41 children, respectively ($p < 0.01$). It should be noted that children in the comparison group did not show positive hearing dynamics after the traditional treatment, the results of CSVI remained unchanged. The given results of clinical observation testify to a reliable improvement of hearing in children of the main group who received complex treatment, which in total showed normalization of hearing on the right in 19.13 ± 1.04 and on the left in 23.50 ± 0.70 cases ($p < 0.001$) (table 3).

To identify the direct or indirect effect of specific IgM and IgG antibodies to toxoplasma and CMV infection on the content of cytokines IL-4, IL-18, LF, C-reactive protein (total and high-sensitivity) in blood, a correlation analysis between the studied parameters after treatment was performed.

The results of correlation analysis after treatment revealed 20 significant correlations: among them 8 full positive, 9 strongly positive and 3 moderately significant correlations (table 4).

It should be noted that after treatment, the correlations of the above parameters were strongly positive, which indicate the effectiveness of our proposed complex treatment.

Table 3. The results of the correlation of the obtained results of SHLHP after treatment in children of the main and comparison groups

Degree of hearing loss	I degree		I-II degree		II degree		II-III degree		III degree		III-IV degree		IV degree		Normal	
	right	left	right	left	right	left	right	left	right	left	right	left	right	left	right	left
Main I group n= 115	38,31 ±1,12	47,31 ±1,12	48,81 ±0,70	58,33 ±0,96	56,52 ±0,75	62,61 ±0,63	62,63 ±0,82	65,53 ±0,54	65,45 ±0,32	72,91 ±0,43	76,57 ±1,00	96,29 ±0,70	94,00 ±1,41	96,00 ±1,41	19,13 ^{***} ±1,04	23,50 ^{***} ±0,70
Comparative group n= 30	28,00 ^{***} ±2,83	37,50 ^{***} ±3,54	39,00 ^{***} ±1,12	50,00 ^{**} ±2,50	46,25 ^{***} ±2,02	51,00 ^{***} ±2,26	52,50 ^{***} ±1,87	60,83 ^{***} ±0,91	61,25 ^{***} ±1,44	68,75 ^{***} ±1,44	67,50 ^{**} ±3,54	80,00 [*] ±7,07	80,71 ^{***} ±2,48	86,43 ^{**} ±2,56	-	-

Table 4. Correlation analysis between specific antibodies and immune status after treatment

	Toxoplasmosis IgM		IgM CMVI		Toxoplasmosis IgG		IgG CMVI	
IL-18 (40- pg/ml)	0,97		1,0		0,97		0,97	
IL-4 (3-8 pg/ml)	0,98		1,0		1,0		1,0	
LF (650-1000 ng/ml)	0,97		1,0		1,0		1,0	
CRP (general) 0-10 mr/l	0,9		0,9		0,8		0,8	
CRP (highly sensitive.) (HsCRP) (0-1 mg/l)	0,8		1,0		0,9		0,9	

Note:

- moderately significant positive correlations
- strongly positive correlations
- full functional correlation relationship.

In modern rehabilitation there are two ways to technically correct hearing loss, depending on the degree of hearing loss. The first is the use of a hearing aid (HA), and in severe forms of hearing loss and deafness, cochlear implantation (CI). In some cases, if toxoplasma and CMV in association play a role in the development of SNHL, a number of peculiarities should be taken into account, firstly, that SNHL may be progressive or have a wave-like course. In our studies, the best result of hearing aids, in particular the use of HA was obtained in children of the main group. The results showed that in 22 (19.1%) children with SNHL in association with toxoplasma and CMV etiology of grade III (60-70 dB), HA was performed. Of 7 (6.1%) patients, 3 (42.9%) with SNHL in association of toxoplasma and CMV etiology of III-IV degree (65-75dB) had hearing correction with HA. In the comparative group, 5 (16.7%) children with SNHL of grade III and 3 (10.0%) children with grade III-IV (65-75db) had hearing aids applied. Despite the results achieved after hearing correction with HA, some of the children in our study showed a lack of progress in speech comprehension and auditory and language skills, which was a direct indication for cochlear implantation (CI).

Of 9 (7.8%) patients in the main group with SNHL of III-IV and IV degrees, 6 (66.7%) patients underwent cochlear implantation (CI) according to the indications after comprehensive treatment, sign language therapy and psychological testing, and special clinical and instrumental examinations. In 3 (33.3%) out of 9 (7.8%) children after HA, active speech and a tendency to hearing improvement were noted, which did not require CI. As noted above, 3 (37.5%) of 8 (26.7%) children in the comparison group diagnosed with grade IV SNHL underwent CI and 5 (62.5%) were included in the state programmer for cochlear implantation. It should be noted that none of the patients had contraindications to cochlear implantation.

4. Conclusions

Those, our studies have shown strong correlations between specific antibodies of pathogens, cytokine status, and inflammatory proteins. The obtained data can be used as therapeutic criteria for SNHL in the association of toxoplasma and CMV infection. Changes in immunological parameters imply the inclusion of antiviral, antioxidant and immune-correcting drugs, the use of which improve clinical signs and laboratory parameters.

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