CASE REPORT

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Results of the Study of the Auditory Analyzer in Newborns with Hyperbilirubinemia

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ABSTRACT

According to statistics, hyperbilirubinemia is observed during the first week of life in approximately 60% of full-term and 80% of premature newborns. It is known that indirect bilirubin has a neurotoxic effect. Accumulation of unconjugated bilirubin in some brain structures may appear to be a temporary or unexpected impairment in auditory, motor, or cognitive function. The narrowing of the OAE spectrum and low amplitude of the response, the increase in the latent periods of III, IV, V peaks, as well as the prolongation of the time of the central sound conduction of the III-V and I-V waves in all newborns with hyperilirubinemia, indicates a pathology of hearing of central origin with impaired conduction along the auditory pathways at the level the lower and middle thirds of the pons of the brain ($P \leq 0.05$).

Keywords: Hyperbilirubinemia, Auditory analyzer, Otoacoustic emission, Brainstem auditory evoked.

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INTRODUCTION

It has been noted that newborns that have had bilirubin encephalopathy at an early age develop dysfunction in the extrapyramidal system, visual impairment, and hearing impairment[1-12]. Several studies have shown that the main site of lesion in the auditory system in hyperbilirubinemia is in the central auditory pathways[2, 3, 6]. However, controversy regarding the location of the lesion stems from other studies that also indicate damage to peripheral auditory structures at the level of hair cells and the auditory (VIII) nerve. According to the interpretation of the co-authors, the severity of damage depends on the degree of hyperbilirubinemia and the duration of its exposure[7-11]. The occurrence on the basal ganglia and nuclei of cranial nerves, including the vestibulocochlear nerve, is especially strong. At the same time, the detection of staining of the basal ganglia, the nucleus of the hypothalamus, the brain stem and the cerebellum of yellow color (kernicterus) cause the deposition of bilirubin in them, which is an important signal of the acute course of the disease. Therefore, assessment of auditory analyzer function in this population should include studies of both the peripheral and central auditory analyzer. According to scientists, hyperbilirubinemia leads to damage to certain areas of the brain[13-17].

The aim of the study is to determine the role of hyperbilirubinemia in the formation of hearing impairment in newborns.

MATERIALS AND METHODS

In total, the study included 60 newborns who were in the intensive care unit and pathology of newborns of the Perinatal Center, which made up the main group. The control group consisted of 20 healthy newborns without somatic pathology (Table 1).

Among the examined were 38 (%) male and 22 (%) females. Gestational age was 35-41 weeks. 42 newborns were born full-term (70.2%), prematurely born (29.8%) newborns. Most parturient women had extragenital pathology of pregnant women: anemia during pregnancy was observed in (85%) mothers; neurocirculatory dystonia in 9, chronic infectious diseases (bronchitis, pyelonephritis, gastritis) were observed in 13 (27%) pregnant. The current pregnancy was complicated by preeclampsia in 24 (48%) people; the threat of termination of a real pregnancy was noted in 16 (40%) women, of which 1-7 % - throughout the pregnancy (Figure 1).

All newborns - 60 children in the examined group of patients were observed with signs of hyperbilirubinemia. All newborns - 60 newborns in the examined group of patients were observed with signs of hyperbilirubinemia. Hyperbilirubinemia as a result of hemolytic disease of the newborn was observed in 32 newborns and hyperbilirubinemia as a result of conjugative jaundice was 28 newborns (Table 2).

In a study, we assessed hearing in neonatal hyperbilirubinemia neonates who were in the intensive care unit. All newborns with hyperbilirubinemia were

Table 1: Neonatal characteristics of the studied children (n = 60).

Index	Values
Male	32 (53.3 %)
Female	28 (46.6 %)
Gestational age (week)	37 (34-40)
Body weight of newborns (grams)	3.210 (1890-4320)
Bilirubin level <256 μmol /l	38 (63.3%)
Bilirubin level >256 μmol /l	22 (36.6%)

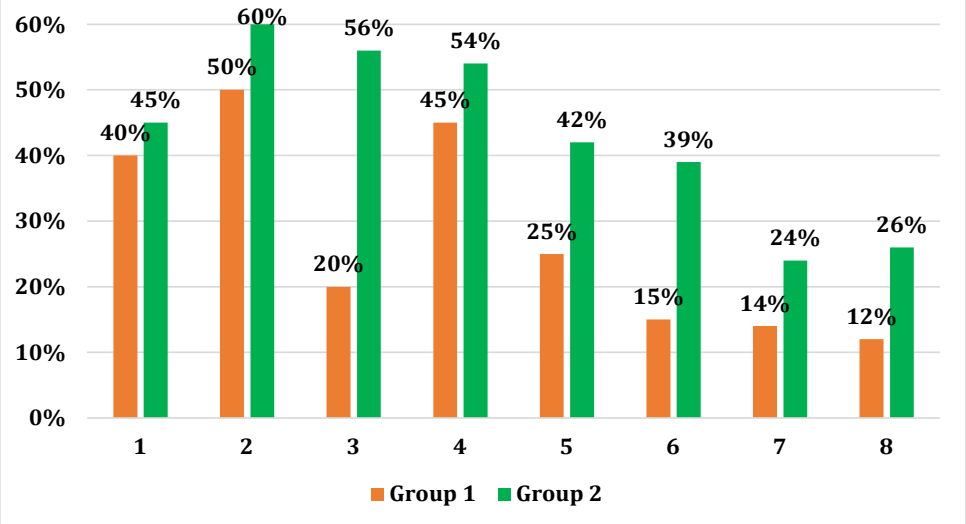

Figure 1: The structure of the pathology of the course of pregnancy and childbirth of mothers of newborns with hyperbilirubinemia.

divided into 2 groups depending on the level of bilirubin in the blood. The first group consisted of 35 newborns with hyperbilirubinemia <256 μmol/l), the second group consisted of 25 newborns with hyperbilirubinemia >256 μmol/l.

On neurological examination Group I revealed the following signs: Moderate muscular hypotension, unstable physiological reflexes, as well as a short tremor of the chin and hands that occurs with anxiety. When examining the brain, no pathological features were identified.

On neurological examination Group II were identified: more persistent muscle hypotension, instability of physiological reflexes, spontaneous Babinsky reflex and Moro reflex, chin tremor, Graefe's symptom. On the basis of neurological symptoms, a syndrome of depression and a syndrome of increased neuro-reflex excitability were identified. Some newborns had no abnormalities on the neurosonogram, and some had areas of induration in the periventricular zone. In the clinical picture of neurological disorders, the syndrome of increased neuro-reflex excitability was predominantly distinguished, as a rule (Table 3).

According to the results of the study of electroencephalography, changes were identified that depended on the degree of the disorder in the range from a slight decrease in the frequency of background activity (8-9 Hz) (in 7 newborns), continuous slow-wave activity (0.5-3 Hz) with spikes and sharp waves (3 newborns), diffuse changes of a cerebral nature (in 1 newborn), and expansion of the ventricular complexes (in 15 newborns).

Neurosonographic study revealed the presence of perinatal hypoxic, hypoxic - hemorrhagic brain damage in the observed children of both groups, as well as signs of benign intracranial hypertension.

RESULTS

All newborns underwent tympanometry with a probing tone frequency of 1000 Hz. When conducting tympanometry, the following results were revealed. Tympanogram type A was registered in all newborns included in the control group. Tympanogram type A was also found in all newborns with perinatal pathology of the central nervous system, which indicates the normal functioning of the middle ear. In our study, the thresholds of the ipsi- and contralateral acoustic reflex were measured at all 4 probed frequencies - 500, 1000, 2000, 4000 Hz. After tympanometry, all newborns were registered in the OAE. In the control group, both classes of OAE were registered in 100% of cases.

All newborns underwent a primary examination using TEOAE. In 25 (%) newborns it was registered within the normal range. The amplitude of TEOAE, averaged over the group, is significantly greater in newborns of the 1st group, compared with the 2nd group in the entire frequency range ($p<0.05$) (Figure 2). It is also noted that the total response power is greater in newborns 1 - th group, compared with newborns of the 2nd group, both on the right and on the left (Figure 3).

From the study, it can be found that in newborns with hyperbilirubinemia, the 1st frequency range, in which TEOAE is recorded, is wider than in newborns with group 2 hyperbilirubinemia. The average number of frequency bands in newborns with from the 1st group is more than 4, and in newborns with hyperbilirubinemia of the 2nd group it is less than 4 both on the left and on the right. A significant difference was obtained in the number of semi-octave frequency bands between the 1st and 2nd groups both on the right ($p<0.001$) and on the left ($p<0.001$) (Table 4.).

In newborns with high levels of hyperbiliubinemia, especially in preterm infants, in most cases of registration of TEOAE, the presence of single peaks, narrowing of the spectrum of the curve and a decrease in cases of their combination, as well as low response amplitude, were observed. In premature newborns with an increase in the level of bilirubin in the blood serum, the registration responses were characterized by a shift in the frequency range to the lower frequency zone. Depending on the degree of damage, a decrease in the amplitude of the maximum peak was also observed. Thus, the frequency analysis revealed a significant difference in DPOAE parameters at frequencies of 5000 and 6000 Hz. At a frequency of 5000 Hz, the average value of the amplitude was 10.26 for the 1st group and 7.87 for the 2nd group in relation to the left ear (Table 5).

At the next stage of the study in newborns with an auditory analyzer, we recorded ABR according to a standard 4-channel recording scheme with monoaural

Table 2: Distribution of patients according to clinical forms of hyperbilirubinemia.

Forms of hyperbilirubinemia	N (%)
Conjugational jaundice	28
Hemolytic jaundice	32

Table 3: Neurological disorders detected in the neonatal period in newborns with hyperbilirubinemia.

Neurological disorders	Group I (N =35)	Group II (N =25)
Intracranial hypertension	25%	23%
Muscular hypotension	12%	22%
Increased neuro-reflex excitability	25%	48%
Weakness of physiological Reflexes	29%	41%
Convulsive syndrome	-	-

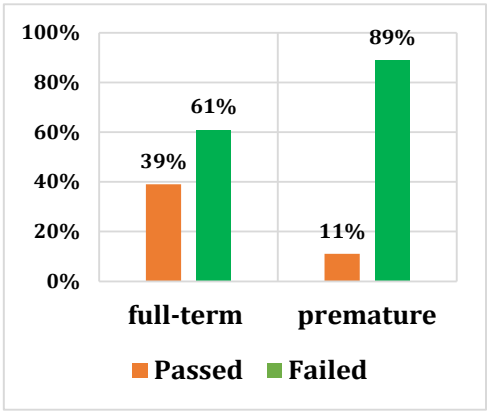

Figure 2: The results of the study of TEOAE in newborns with group I hyperbilirubinemia.

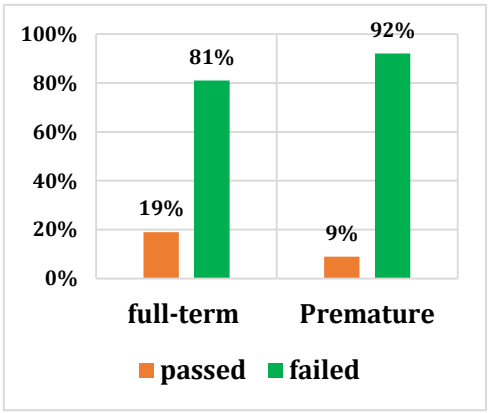

Figure 3: Results of the study of TEOAE in newborns with perinatal asphyxia of group II.

Table 4: Description of the signal-to-noise ratio variable TEOAE (in dB SPL) in newborns with hyperbilirubinemia.

Indicator, Hz	Group I (N= 38)		Group II (N=22)		Control group (N=20)	
	right ear	left ear	right ear	left ear	right ear	left ear
1000	4.20±1.58*	4.94±1.27*	3.30±1.20*	2.44±1.49*	8.71±0.76	8.37±0.72
2000	5.41±1.23*	4.95±1.48*	5.82±1.22	3.35±1.21*	8.59±0.67	7.61±0.78
3000	6.44±0.97	3.99±1.23*	3.91±0.95*	3.51±1.31*	6.47±0.73	6.23±0.70
4000	7.21±0.99*	6.50±1.05*	8.16±1.26*	8.5±1.78*	13.54±0.71	12.74±0.60
5000	5.93±1.08*	6.95±0.95*	6.23±1.43*	7.8±1.51*	11.89±1.05	12.32±1.35

Note: * - significant difference according to Student's t-test at $p \leq 0.05$ in relation to the control group.

Table 5: Comparative characteristics of the results of registration of ABRs in newborns of the I group by sex.

Index	N	M	I group Standard deviation	N	AND	Standard deviation	P
Wave I	34	1.61	0.34	38	1.54	0.23	0.7696
Wave III	34	4.05	0.30	38	3.98	0.29	0.2904
Wave V	34	6.27	0.42	38	6.14	0.42	0.1817
Peak Interval I - III	34	8.29	0.24	38	8.17	0.35	0.0888
Interpeak interval III-V	34	2.22	0.42	38	2.16	0.28	0.1496
Peak Interval IV	34	4.65	0.42	38	4.6	0.40	0.6652

Note: * - significant difference according to Student's t-test at $p \leq 0.05$ in relation to the control group.

click stimulation at a stimulus intensity of 80–90 dB. In the course of the study, such parameters of the extracted components as latencies and maximum wave amplitudes were evaluated.

The absolute delays of waves I, III, and V, as well as the inter-wavelength delays of waves I-III, III-V, and IV, were measured at 90 dB. To determine the hearing threshold for the V wave, stimulus intensity was lowered by 20 dB intervals. The criterion for normal hearing was the presence of the V wave at a stimulus intensity of 20 dB (Table 6).

Comparison of waves I, III, and V of absolute and latency interactions in our study sample did not reveal statistically significant gender differences across all tested intensities.

Latent periods of the 1st peak in newborns of the 1st group were 1.97 ± 0.21 ms on the left, 1.96 ± 0.27 ms on the right; in newborns of the 2nd group, it was 2.34 ± 0.12 ms on the left, 1.87 ± 0.18 ms on the right, which is a statistically significant result; In newborns of the control group, the periods of the 1st peaks were on the right 1.9 ± 0.21, on the left 1.8 9 ± 0.15 ms (Table 7).

The average value in the values of the latent periods of III peaks in newborns of the 1st group was 4.62 ± 0.41 ms; in newborns of the 2nd group was 4.56 ± 0.4 m s, which is a statistically significant indicator. The average value in the values of the latent periods of V peaks in newborns of the 1st group was 6.74 ± 0.44 ms; in newborns of the 2nd group, latency prolongation was noted, which was 7.2 ± 0.41 ms on the left, which is a statistically significant indicator (Table 8).

The value of interpeak intervals IV for the 1st group was 4.79 ± 0.39 ms., and the intervals for the 2nd group were 5.15 ± 0.52 ms on the left, respectively. The results of registration of ABR showed statistically significant differences when comparing the absolute delays for waves I, III and V at 80 dB between 1-2 groups of newborns; lower values were found in neonates with high bilirubin levels compared to those with moderate bilirubin levels. Longer V delays were found at 40 dB/h in neonates from group 2, which are statistically significant. Interpeak I-III, III-V and IV intervals were more prolonged in newborns with severe hyperbilirubinemia, which is statistically significant. According to the results, the increase in the latent periods of III, IV, V peaks, as well as the prolongation of the time of the central sound conduction of III-V and IV in all newborns with hyperilirubinemia, indicates a hearing pathology of central origin.

In order to determine the level of damage to the auditory analyzer, registration of long-term ABR was carried out. An analysis was made of the latency, the amplitude of the peaks of the long-term ABR. The latency of the long-term AB waves characterizes the degree of activity of neurons during stimulation, and the amplitude characterizes the number of excited neurons (Table 9).

According to the results of registration of long-term ABR, an increase in the latency of long-term ABR indicators in newborns with hyperbilirubinemia was revealed, which is a significant difference from the indicators of the group of newborns with asphyxia and the control group. The indicators of long-term ABR in newborns with asphyxia in relation to the amplitude of the peaks tended to decrease their values, but the difference from the control indicators was not statistically significant.

Thus, despite the predominant damage to the peripheral part of the auditory analyzer, according to the registration of long-term ABR, the presence of deviations in the cortical

Table 6: Comparative characteristics of the results of registration of ABRs in newborns of II group by sex.

Index	II group			AND			P
	N	M	Standard deviation	N		Standard deviation	
Wave I	24	1.73	0.37	36	1.69	0.33	0.7235*
Wave III	24	4.2	0.29	36	4.10	0.29	0.2199
Wave V	24	6.53	0.28	36	6.35	0.41	0.0786*
Peak Interval I - III	24	8.38	0.32	36	8.32	0.28	0.1013
Interpeak interval III-V	12	2.25	0.4	18	2.39	0.35	0.3155
Peak Interval IV	12	2.69	0.35	18	2.43	0.38	0.0744

Note: * - significant difference according to Student's t-test at p ≤ 0.05 in relation to the control group

Table 7: Comparative characteristics of the results of registration of ABRs in newborns of the study groups.

Options KSVP	Group I Average meaning	Group _ II Average value	Control group	Meaning P
I Right ear	1.97±0.21	1.99±0.28	1.8±0.21	0.46
I Left ear	1.95±0.23	2.11±0.32	1.8±0.15	0.01 *
III Right ear	4.62±0.41	4.56±0.4	4.4±0.23	0.49
III Left ear	4.65±0.35	4.61±0.44	4.4±0.31	0.63
V Right ear	6.74±0.44	7.14±0.5	6.6±0.32	0.0001*
V Left ear	6.87±0.39	7.2±0.41	6.6±0.13	0.0002*
Peak interval IV Right ear	4.79±0.39	5.15±0.52	2.11±0.15	0.0003*
Peak interval IV Left ear	4.91±0.39	5.09±0.39	2.11±0.15	0.03*

Note: * - significant difference according to Student's test p ≤ 0.05 in relation to the control group.

Table 8: Neonatal characteristics of newborns of the studied groups by gestational age.

Indicators	35 weeks	36 weeks	37 weeks	>3 8 weeks
Group I (N=35)	10	4	9	12
Group II (N=25)	9	5	5	6
Control group (N=20)	-	-	-	20

Table 9: The duration of the icteric period in children with hyperbilirubinemia.

Duration of the icteric period (in days)	gestational age			
	Group I		Group II	
	term	premature	term	premature
up to 10 days	-	-	-	-
10-14 days	11	10	5	7
14 - 21 days	1	13	1	12

Table 10: Indicators of TEOAE of newborns of the studied groups in dynamics.

	Groups	1-7 day	3 months	6 months	12 months
2 Hz	Group I	5.66	8.0	11.2	12.81
	Group II	5.13	7.8	10.38	12.13
	Control group	8.01	10.38	11.15	12.38
3 Hz	Group I	4.48	8.1	10.30	11.39
	Group II	3.83	8.7	9.09	10.37
	Control group	7.05	10.21	11.89	12.34
4 Hz	Group I	9.78	11.3	11.9	12.01
	Group II	9.30	9.9	10.34	11.3
	Control group	11.13	12.78	12.80	12.81
5 Hz	Group I	10.26	10.99	11.76	12.05
	Group II	7.87	8.08	10.01	11.23
	Control group	12.84	12.84	12.88	12.80
6 Hz	Group I	11.29	11.33	12.45	12.61
	Group II	5.20	8.09	10.55	11.01
	Control group	12.81	12.81	12.34	12.80

section of the auditory analyzer in a group of newborns with a high level of bilirubin in the blood was also revealed. For a dynamic study of auditory function, the study was carried out at periods of 3 months of life, 6 months of life and 12 months of life. The control group consisted of 20 full-term newborns, who were also examined in similar periods of life.

As a result of the study of newborns with hyperbilirubinemia, there was a fluctuation in the percentage of detected pathology in the study groups, depending on the duration of the examination (Table 10).

DISCUSSION

In a study, we assessed hearing in neonatal hyperbilirubinemia neonates who were in the intensive care unit. All newborns with hyperbilirubinemia were divided into 2 groups depending on the level of bilirubin in the blood. The first group consisted of 35 newborns with hyperbilirubinemia <256 μmol/l), the second group consisted of 25 newborns with hyperbilirubinemia >256 μmol/l.

Clinical signs of jaundice began to appear from the first day of life in 12 children born with signs of hemolytic disease of the newborn and the level of indirect bilirubin in the umbilical cord blood, another 9 newborns with signs of liver immaturity and elevated serum bilirubin. In the rest of the newborns, clinical signs of hyperbilirubinemia began to appear from the 3rd day of life.

Neurological examination of newborns of the 1st group revealed such signs as: moderate muscular hypotension, inconsistency of physiological reflexes, as well as a short tremor of the chin and hands that occurs with anxiety. At examination of the brain revealed no pathological features. Neurological examination of newborns of the 2nd group revealed such signs as: persistent muscle hypotonia, inconsistency of physiological reflexes, spontaneous Babinski reflex, Moro reflex, chin tremor, Graefe's symptom were determined. Some newborns from this group had no special abnormalities in neurosonography, and some newborns were determined areas of seals in the periventricular zone. No neurological abnormalities were noted in the control group.

Evaluation of neurological disorders in newborns with hyperbilirubinemia over time showed that in most of them (in 96.1%), stabilization of the neurological status occurs by the age of 1 year. The most common were intracranial hypertension - 25-33% and increased neuro-reflex excitability - 25-48%, for which newborns were treated at the time of the study. At 3 and 6 months of life, the syndrome was detected in 12-22% of newborns. We also identified muscle hypotension -12-22%, and weakness of physiological reflexes - 29-41%, which are most of the children with these syndromes identified at the age of 3 months, by 6 months the number of such children has significantly decreased - up to 5-7 % ($p<0.01$), and at 12 months it was detected - 1% (Figure 4).

When registering TEOAE on days 1-7 of life, we observed the presence of TEOAE in 89% of full-term newborns of the 1st group and 65% of premature newborns of the 2nd group with a gestational age of 35-37 weeks. The absence of registration of TEOAE was observed in 12% of full-term newborns of the 1st group and 35% of premature newborns of the 2nd group with a gestational age of 35-37 weeks (Figure 5).

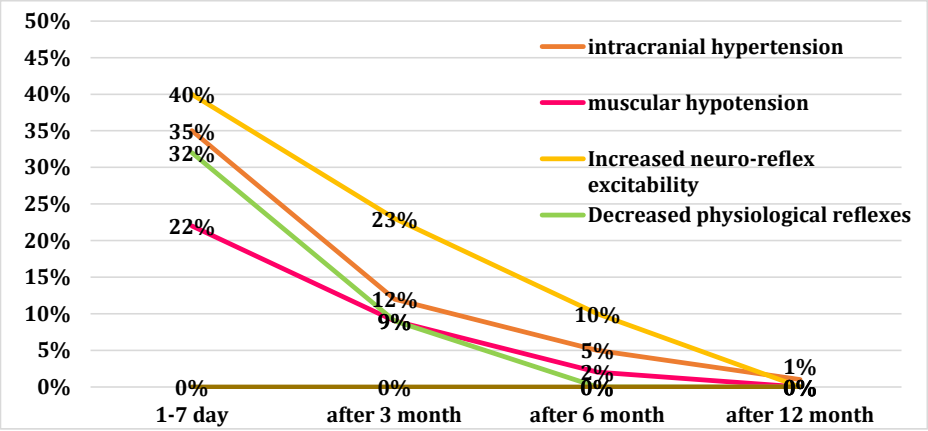

Figure 4: Clinical neurological disorders and outcomes in newborns with hyperbilirubinemia in dynamics.

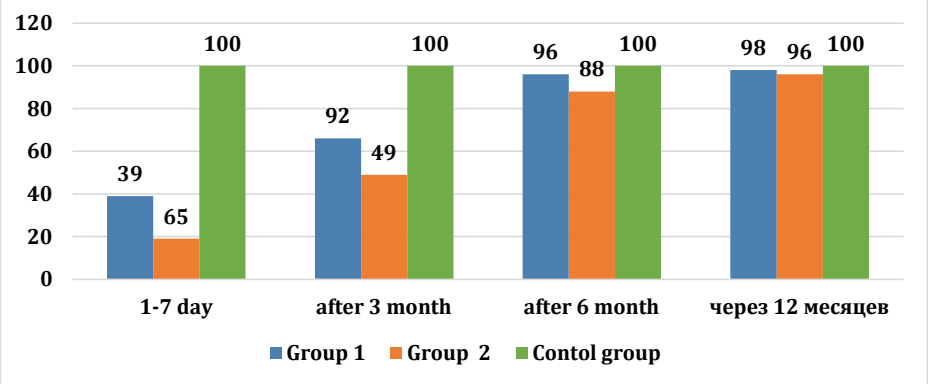

Figure 5: Indicators of TEOAE of newborns of the studied groups in dynamics.

At 3 months of life, the highest response power among the two groups was registered in the 1st group, which amounted to 92%, and in the 2nd group it was 88%.

Newborns who did not register TEOAE on days 1-7 of life belonged to group 2 with a gestational age of 35-36 weeks. Although there were differences in mean amplitude among study groups, neonates were analyzed to present responses within the expected normal range, with amplitude greater than or equal to -5 dB. Regarding the difference in response amplitude between the ears, it was noted that in all groups, both ears showed results without significant differences in the change in the average amplitude.

When analyzing the results, no statistically significant differences were found between the groups. However, lower p values were observed in newborns of both groups, especially group 2, at high frequencies - 5 kHz and 6 kHz, which indicates a trend towards an increase in TEOAE amplitudes at higher frequencies, corresponding to the function of the base of the cochlea. Lifetime TEOAE amplitude results showed smaller response amplitudes in neonates with severe hyperbilirubinemia. TEOAE surveys conducted at 3, 6 and 12 months. Life showed an increase in amplitudes with increasing gestational age.

CONCLUSION

From the study, it can be found that in newborns with hyperbilirubinemia, the 1st frequency range, in which OAE is recorded, is wider than in newborns with group 2 hyperbilirubinemia. The average number of frequency bands in newborns with from the 1st group is more than 4, and in newborns with hyperbilirubinemia of the 2nd group it is less than 4 both on the left and on the right. A significant difference was obtained in the number of semi-octave frequency bands between the 1st and 2nd groups both on the right ($p<0.001$) and on the left ($p<0.001$).

The narrowing of the ABR spectrum and low amplitude of the response, the increase in the latent periods of III, IV, V peaks, as well as the prolongation of the time of the central sound conduction of the III-V and I-V waves in all newborns with hyperilirubinemia, indicates a pathology of hearing of central origin with impaired conduction along the auditory pathways at the level the lower and middle thirds of the pons of the brain ($P \leq 0,05$).Thus, the use of a full arsenal of objective studies is the most effective and reliable strategy for the rapid and accurate diagnosis of hearing impairment in newborns and young children.

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