UDC 616.831-009.11-053.2

K.V. Yatsenko, V.A. Berezovskii, J.V. Deyeva

Effects of intermittent normobaric hypoxia on the state of the CNS and cerebral circulation in children with cerebral palsy

We studied the effects of intermittent normobaric hypoxia (INH) on the processes of CNS functions and cerebral circulation recovery in children with cerebral palsy (CP). Altogether, 87 patients (from 8.5 months to 12 years) with CP were examined and received the course of treatment. Clinico-neurophysiological examination was performed before the treatment and immediately after termination of the therapeutic course. Patients were divided into two groups; age and sex distributions and clinical manifestations of CP were randomized. The comparison group was formed from 34 children who received the course of the generally accepted complex therapy (medicamental treatment, massage, Bobat-therapy, Vojta-therapy at al).. The main group included 53 patients who, in addition to the same therapy, were exposed to INH using an individual apparatus for artificial mountain air, Borey-M, made in the Scientific Medico-Engineering Center NORT (Ukrainian National Academy of Sciences, Kyiv). Children of the main group were exposed to the dosed normobaric sanogenetic level hypoxia intermittently once per day. For this purpose, we used a normobaric gas hypoxic mixture (12% O_2 + 88% N_2). Each cycle included a 15-min-long episode of breathing with the gas mixture alternated by a 5-min-long episode of breathing an ambient atmospheric air. The number of hypoxic cycles was gradually increased (from one to three). The entire course of treatment included, on average, 10 sessions. After complex therapy the stable positive effects on the motor status were observed in 94% of patients of the main group (exposed to INH) and in 74% of patients of the comparison group (unexposed to INH). EEG examination showed that positive dynamics of spectral EEG components were in 70% of patients of the main group and in 56% of children of the comparison group. Doppler examination showed that brain hemodynamics was normalized in 85% of patients of the main group and in 59% of children of the comparison group. In the course of ophthalmoscopic examination, we found that the dynamics of indices of the state of the eye fundus were expressed more clearly in children of the main group than in patients of the comparison group (in 32 and 12% of patients, respectively).
Key words: cerebral palsy, intermittent normobaric hypoxia, adaptation.

INTRODUCTION

There are some outstanding questions in the functioning of the CNS of animals and humans that remain to be answered. The question of the recovery of CNS functions impaired by congenital abnormalities remains open and deserves special attention. In the course of embryogenesis, there are periods when the embryo is highly sensitive to different factors that can disturb the genetic program of development; there are also critical periods for different organs. The brain and skeleton are sensitive to injurious influences permanently, beginning from the 3rd week of impregnation to the end of pregnancy. In the current state of nosology, syndromes resulting from the abnormal development of the brain or its damage within the pre-, intra-, and early postnatal periods are grouped and defined as CP. The incidence and prevalence rates from CP in children vary from 1.5 to 2.6 per 1.000 population. Diseases of the CNS (in particular CP) are main reasons for childhood disability [18-19]. As the published data indicate, the effects of pathogenic factors on the formation of the nervous system of a child within the pre-,

© K.V. Yatsenko, V.A. Berezovskii, J.V. Deyeva

intra-, and postnatal periods play a crucial role in the development of CP. Specific pathological changes in the motor sphere (disorders of elementary movements via spasticity, rigidity, dystonia, or hypotonia of separate muscles or muscles functionally combined in muscular synergism) are leading manifestations of CP [8].

The existing methods for the recovery of physiological functions impaired by CP are aimed at pharmacological and reflectory stimulation of physiological regeneration of the CNS cells capable of differentiating. It was demonstrated that neurogenic stem units exist in certain regions of the brain and spinal cord and can migrate and develop; these fully differentiated cells restore the quantitative composition of the injured neuronal networks [5]. In modern medicine, more and more attention is being paid to the problem of physiological regeneration and also to the search for pathways of stimulation of this regeneration in the human organism. The search for novel pathways of activation of the processes of recovery of disturbed CNS functions, which can intensify the effectiveness of therapy via stimulation of natural mechanisms underlying sanogenesis and, at the same time, can be combined with other conventional techniques (but cannot induce undesirable consequences), is urgent. The method of intermittent normobaric hypoxia (INH) based on the activation of defensive mechanisms and physiological reserves of the human organism can be one of the above pathways [1-3, 10, 17].

Intensification of the processes of regeneration of the cells under conditions of training to moderate hypoxia seems to be the most promising technique for treatment and rehabilitation of children with CP. The recovery of the neuronal pool can become the basis for sanogenic effect of a dosed decrease in the partial pressure of oxygen on the pathogenesis of CP.

METHODS

To estimate the effectiveness of rehabilitation of children with CP (who received the complex therapy combined with sessions of INH), we studied the dynamics of clinico-neurophysiological picture using clinico-neurological, neurophysiological (EEG), transcranial Doppler (TCD), ophthalmoscopic, and statistical techniques.

Altogether, 87 patients (from 8.5 months to 12 years) with CP were examined and received the course of treatment. Clinico-neurophysiological examination was performed before the treatment and immediately after termination of the therapeutic course.

Patients were divided into two groups; age and sex distributions and clinical manifestations of CP were randomized. The comparison group was formed from 34 children who received the course of the generally accepted complex therapy (medicamental treatment, massage, Bobat-therapy, Vojta-therapy at al). The main group included 53 patients who, in addition to the same therapy, were exposed to INH. All studies were ratified and done with the orservance of international ethic norms [11].

In the Ukrainian Medical Center for rehabilitation of children with organic lesion of the nervous system (Ministry of Public Health of Ukraine, Kyiv), where we carried out a clinical examination, reasonably healthy children of the corresponding ages are not examined using the techniques applied in our work. To estimate the level of deviation of the studied indices from the physiological norm, we referred to the respective data published by other researchers [6-7, 13-14].

To diagnose CP, we used the clinical classification of CP proposed by Semenova [9]. The level of development of gross motor functions was evaluated in each child according to the Gross Motor Function Classification System (GMFCS) for cerebral palsy [20].

The initial motor status of children with CP was evaluated by seven articles of the five-point scale. The following indices of the motor status were taken into account: paresis, hypertonus, limitation of the range of active movements, pathological purposes, pathological reflexes, hyperkineses, and discoordinated disorders. Each index was estimated in points (from one to five) depending on the degree of pathological manifestations; one point corresponded to

the norm, while five points corresponded to the maximal motor dysfunction [12].

Taking into account a trend toward formation of EEG variants in children, we analyzed EEG using the respective classification proposed by Zhirmunskaya [4]. To examine the spectral power densities (SPDs) of EEG frequency ranges, we used the data of spectrum-amplitude mathematical transformation of the analog ЕЕГ (results of Fourier analysis of initial EEG data).

To reveal objective signs of pathology of cerebral hemodynamics in children with CP, the analysis of results of transcranial Doppler (TCD) examination was performed using isolated specific Doppler patterns. For evaluating the level of disturbance of cerebral hemodynamics and the state of cerebral blood flow through the main arteries and veins, we used the asymmetry coefficient (AC) of blood flow velocities in the middle and anterior cerebral arteries (MCA and ACA, respectively). In the course of examination of patients with CP, we also used a velocity TDC parameter (mean flow velocity, MFV) for evaluating the cerebral arteries (basilar artery, BA, as well as the MCA and ACA) [15].

Ophthalmologic examination of patients with CP was performed using the conventional technique [16].

Children of the main group were exposed to the dosed normobaric sanogenetic level hypoxia intermittently once per day. For this purpose, we used a normobaric gas hypoxic mixture (12% O_2 + 88% N_2). Each cycle included a 15-min-long episode of breathing with the gas mixture (12% O_2 + 88% N_2) alternated by a 5-min-long episode of breathing an ambient atmospheric air. The number of hypoxic cycles was gradually increased (from one to three). The entire course of treatment included, on average, 10 sessions.

The course of INH was performed using an individual device for artificial mountain air, Borei-M, made in the Scientific Medico-Engineering Center NORT (National Academy of Sciences of Ukraine, Kyiv, Ukraine).

To estimate individual sensitivity, each patient was asked to perform a test session of breathing a 14% O_2-containing gas mixture before the treatment using a helmet. The duration of the test session was 10 min long. Control measurements were performed prior to and after each session. Results of test sessions were evaluated according to the step scale. Based on the obtained data, individual regime of INH was prescribed to hypoxic loading.

To evaluate the objective effectiveness of the above-described therapy for each group under examination, we used the technique for estimation of significant differences of means of independent samplings with the help of Student's t-test. Significance of differences was estimated using the t-test at $P < 0.05$.

RESULTS AND DISCUSSION

According to our clinico-neurophysiological examination of children with CP, which was performed after the course of generally used complex therapy combined with the course of INH, the stable positive effects on the motor status were observed in 94% of patients of the main group (exposed to INH) and in 74% of patients of the comparison group (unexposed to INH).

In children of the main group, we observed a significant increase in the range of active movements, decreases of clinical manifestations of paresis and pathological purposes, reduction of hypertonus, and decreases of manifestations of hyperkineses and discoordinated disorders. In patients of the comparison group, differences between some indices of the motor status before and after treatment were significant (expression of hypertonus decreased, range of active movements increased, and discoordinated disorders decreased).

The comparison of clinical findings showed that the therapeutic effects were significantly higher in children of the main group. In this group, some indices of the motor status demonstrated significant differences (we found decreases in the degree of manifestation of paresis, pathological purposes, hyperkineses, and discoordinated disorders). In patients of the comparison group, changes in the motor status were insignificant (Tab. 1).

TABLE 1. Comparative characteristics of the effectiveness of rehabilitation of children with cerebral palsy

Studied groups	Indices of the motor status (points)						
	paresis	hypertonus	limitation of the range of active motions	pathological purposes	pathological reflexes	hyperkine-ses	discoordinated disorders
Children who received the course of generally used complex therapy (comparison group, n = 34):							
before treatment	3.0±0.12	3.35±0.16	3.18±0.16	2.97±0.12	2.59±0.16	2.59±0.16	3.35±0.12
after treatment	2.88±0.12	2.70±0.12*	2.70±0.16*	2.97±0.12	2.59±0.16	2.53±0.16	3.10±0.12
Δ%	−4.0	−19.4	−15.0	0.00	0.00	−2.30	−7.50
Children who received the course of generally used complex therapy combined with the course of intermittent normobaric hypoxia (main group, n = 53):							
before treatment	3.43±0.09	3.77±0.12	3.20±0.12	3.15±0.09	3.0±0.09	2.75±0.09	2.77±0.12
after treatment	2.94±0.09*	2.92±0.12*	2.58±0.09*	2.88±0.09*	3.0±0.09	2.22±0.09*	2.15±0.09*
Δ%	−14.3	−22.6	−19.4	−8.6	0.00	−19.3	−22.4

Footnote. Asterisks show cases of significant ($P < 0.05$) differences of the studied indices in children after therapeutic treatment in compare with before treatment

Therefore, the used combined complex therapy promotes the positive clearly pronounced dynamics of the motor status of children with CP. Positive changes were manifested in an increase in the range of active movements (in 66 and 50% of patients of the main and comparison groups, respectively), overcoming of pathological synergies (32 vs 9%), and reduction of the muscle tone of spastic muscles (76 vs 52%).

As EEG examination showed, the used course of INH resulted in decreases in the pathologically disorganized and hypersynchronized EEG patterns by 12 and 4%, respectively. The comparison group demonstrated no such trend (Fig. 1).

In children exposed to INH, the SPD of the alpha rhythm significantly increased by 23%, while the comparison group demonstrated a significant rise in the SPD of this rhythm only by 13%. In both the examined groups, we also observed a significant increase in the SPD of the beta range (by 26% in patients of the main group and only by 19% in children of the comparison group). In children of the main group, SPDs of delta and theta rhythms significantly decreased by 35%, while the comparison group, according to the data of Fourier analysis, demonstrated no significant changes in these EEG ranges (Tab. 2).

The comparison of the obtained data showed that positive dynamics of spectral EEG components were expressed more clearly in children of the main group than in patients of the comparison group. The main group demonstrated a significant rise in the SPD of the alpha rhythm and a significant decrease in the SPD of delta waves, while changes in the EEG characteristics observed in the comparison group were insignificant.

Doppler examination showed that brain hemodynamics was normalized in 85% of patients of the main group and in 59% of children of the comparison group. The AC of blood flow velocity in the MCA decreased 3.4 times in children of the main group, while in patients of the comparison group this index decreased only 1.3 times (Tab. 3). In the ACA, the above coefficient decreased 2.7 and 1.1 times in children of the main and comparison groups, respectively.

In patients of the main group, high flow velocities in the BA, MCA, and ACA demonstrated significant decreases (20, 14, and 6%, respectively). In the comparison group, we also observed positive dynamics of these indices, but changes were insignificant.

In children exposed to INH, low flow velocities in the BA, MCA, and ACA demonstrated significant increases (27, 19, and 9%, respectively), while in patients of the comparison group, only the MCA velocity increased significantly (10%).

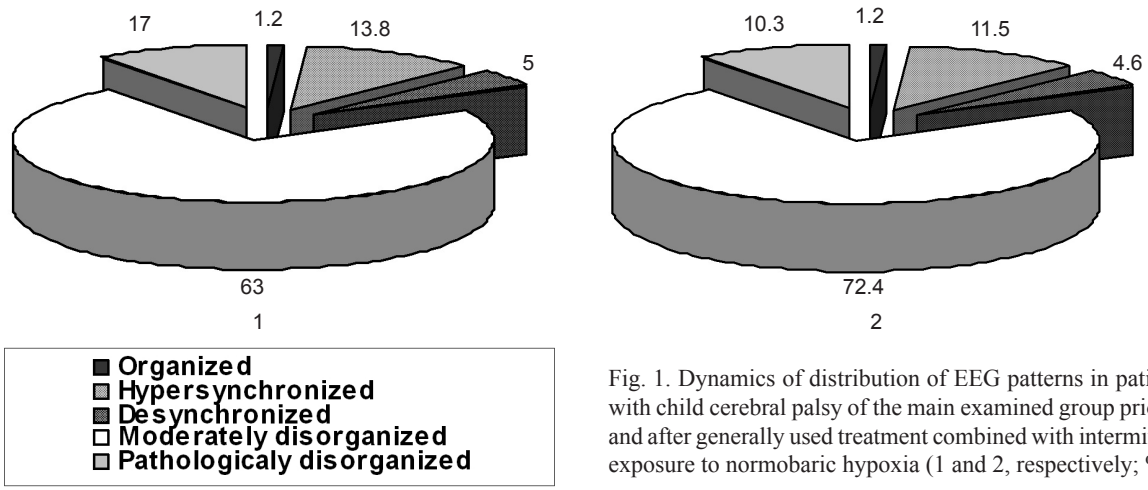

Fig. 1. Dynamics of distribution of EEG patterns in patients with child cerebral palsy of the main examined group prior to and after generally used treatment combined with intermittent exposure to normobaric hypoxia (1 and 2, respectively; %)

TABLE 2. Results of Fourier analysis of EEG recorded from children with cerebral palsy

Examined children	Spectral power densities of EEG frequency ranges (μV^2/Hz)			
	alpha	beta	delta	theta
Main group (n = 53)				
before treatment	55.0±3.34	14.5±0.95	196±7.4	202±12.4
after treatment	71.0±2.86*	19.6±0.95*	128±8.0*	132±5.7*
Δ%	+22.5	+26	−34.7	−34.7
Comparison group (n = 34)				
before treatment	45.0±2.5	16.3±1	194.5±11.4	169±9.98
after treatment	51.8±2.5*	20.0±1*	173±10.3	145±8.98
Δ%	+13	+18.5	−11	−14.2

Footnote. Asterisks show cases of significant ($P < 0.05$) differences prior to and after treatment

The comparison of the data obtained in the course of TCD examination showed that positive dynamics of Doppler patterns suggestive of mean flow velocities in the studied cerebral arteries were expressed more clearly in patients exposed to INH than in patients of the comparison group. In patients of the main group, both increases and decreases in the MFV in the BA, MCA, and ACA were significant. At the same time, the comparison group demonstrated a significant rise in the MFV only in the BA and MCA (Fig. 2).

In the course of ophthalmoscopic examination, we found that the dynamics of indices of the state of the eye fundus were expressed more clearly in children exposed to INH (main group) than in patients of the comparison group (in 32 and 12% of patients, respectively). Positive changes were manifested in (i) a decrease in the number of cases of stenosis of retinal vessels (5 times in children of the main group and only 1.4 times in patients of the comparison group), (ii) a 2-fold decrease of manifestations of angiospasm of the retina observed in the main group (while the comparison group demonstrated no changes in this index), and (iii) an increase in the number of vessels at the periphery of the retina (4.5 and 1.6 times in the respective groups) (Fig. 3).

CONCLUSION

After complex therapy the stable positive effects on the motor status were observed in 94% of patients of the main group (exposed to INH) and in 74% of patients of the comparison group (unexposed to INH). EEG examination showed that positive dynamics of spectral EEG components were in 70% of patients of the main group and in 56% of children of the comparison group. Doppler examination showed that cerebral hemodynamics was normalized in 85% of patients of the main group and in 59% of children of the comparison group. In the course of ophthalmoscopic examination,

TABLE 3. Results of transcranial Doppler examination of children with cerebral palsy

Examined children	Asymmetry coefficient of blood flow velocities	
	in the middle cerebral artery (%)	in the anterior cerebral artery (%)y
Comparison group (n = 34)		
before treatment	16.2	11.7
after treatment	12.5	11.0
Δ%	3.7	0.7
Main group (n = 53)		
before treatment	18.5	15.3
after treatment	5.4	5.5
Δ%	13.1	9.8

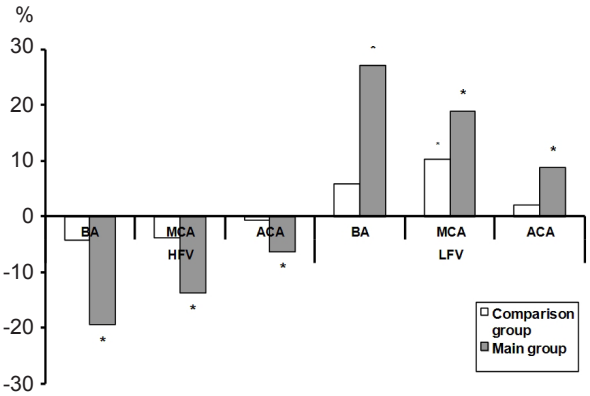

Fig. 2. Changes in cebral hemodynamics observed in two groups of children with cerebral palsy after the corresponding treatments. Vertical scale mean flow velocity in cerebral arteries, %. HFV and LFV are, respectively, high and low flow velocities basilar artery (BA), middle and anterior cerebral arteries (MCA, ACA) respectively. Asterisks show cases of significant ($P < 0,05$) differences from the corresponding values of flow velocities before treatment

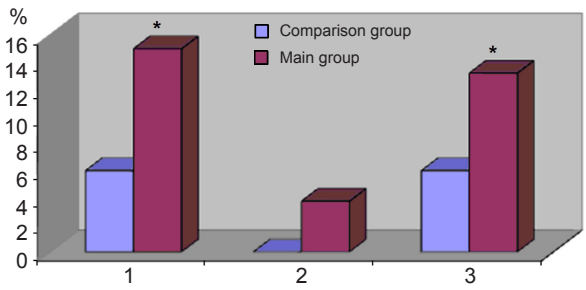

Fig. 3. Dynamics of indices of the state of the eye fundus in children with cerebral palsy of the examined main and comparison groups. Vertical scale: changes in the number of cases where positive dynamics were observed, %. 1-3: decreases of manifestations of stenosis of retinal vessels (1) and angiospasm of the retina (2), and increase in the number of vessels at the periphery of the retina (3). Asterisks show cases of significant ($P < 0.05$) differences from the corresponding indices before treatment

we found that the dynamics of indices of the state of the eye fundus were expressed more clearly in children of the main group than in patients of the comparison group (in 32 and 12% of patients, respectively).

Neurophysiological, EEG, TCD, ophthalmoscopic, CNS state indices and cerebral circulation indicate that intermittent exposure to the dosed normobaric sanogenetic level hypoxia combined with the generally accepted therapy (used for rehabilitation of children with CP) results in a significant intensification of the processes the brain deficiency reparation and also in the improvement of the CNS-controlled motor and mental functions in these patients.

Е.В. Яценко, В.А. Березовский, Ю.В.Деева

ДЕЙСТВИЕ ПРЕРЫВИСТОЙ НОРМОБАРИЧЕСКОЙ ГИПОКСИТЕРАПИИ НА СОСТОЯНИЕ ЦНС И МОЗГОВОГО КРОВООБРАЩЕНИЯ У ДЕТЕЙ С ЦЕРЕБРАЛЬНЫМ ПАРАЛИЧОМ

Исследовали эффективность действия прерывистой нормобарической гипоксии (ПНГ) на состояние ЦНС и мозгового кровообращения у детей с церебральным параличом (ДЦП). Проведено комплексное обследование и лечение 87 детей с ДЦП в возрасте от 8,5 мес до 12 лет. Клинико-нейрофизиологическое обследование проводилось до лечения и сразу же по окончании терапевтического курса. Пациенты были разделены на две группы рандомизированные согласно возрасту, полу, клинической форме ДЦП. Первая группа (сравнения) состояла из 34 детей, которым проводили традиционную комплексную терапию (медикаментозное лечение, массаж, Бобат-терапия, Войта-терапия и др.). Основная группа (53 пациента) на фоне общепринятой комплексной терапии дополнительно проходила курс ПНГ с помощью индивидуального аппарата горного воздуха типа «Борей-М» (производства Научно-исследовательского медико-инженерного центра НОРТ НАН Украины, г. Киев). Для ПНГ использовали нормобарическую газовую гипоксическую смесь (ГГС-12), которая состояла из 12 % кислорода и 88 % азота. Сеансы проводились один раз в день в интермиттирующем режиме: 15 мин – дыхание ГГС-12, 5 мин – атмосферным воздухом (один цикл). Количество циклов увеличивалось от одного до трех. Курс ПНГ в среднем состоял из 10 сеансов. После проведенного комплексного лечения положительная динамика в двигательном статусе отмечалась у 94 % детей основной (с применением ПНГ) группы и у 74 % группы сравнения. Электроэнцефалографическое обследование пациентов обеих групп выявило позитивные изменения у 70 % детей основной группы и у 56 % группы сравнения. Транскраниальная допплерография сосудов головного мозга установила наличие положительной динамики у 85 % детей основной группы и у 59 % группы сравнения. При проведении офтальмоскопического исследования позитивные изменения в состоянии глазного дна отмечались у 32 % пациентов основной группы и у 12 % группы сравнения.

Ключевые слова: детский церебральный паралич, прерывистая нормобарическая гипоксиия, адаптация.

К.В. Яценко, В.Я. Березовський, Ю.В.Дєєва

ДІЯ ПЕРЕРИВЧАСТОЇ НОРМОБАРИЧНОЇ ГІПОКСІЇ НА СТАН ЦНС І МОЗКОВОГО КРОВООБІГУ У ДІТЕЙ З ЦЕРЕБРАЛЬНИМ ПАРАЛІЧЕМ

Досліджували ефективність дії переривчастої нормобаричної гіпоксії (ПНГ) на стан ЦНС та мозкового кровообігу у дітей хворих на церебральний параліч (ДЦП). Обстежено та комплексно проліковано 87 хворих на ДЦП віком від 8,5 міс до 12 років. Клініко-нейрофізіологічне обстеження проводили до лікування та по закінченні курсу терапії. Пацієнти були розподілені на дві групи, рандомізовані за віком, статтю, клінічною формою ДЦП. Першу (порівняльну) групу складали 34 особи, яким проводили традиційну комплексну терапію (медикаментозне лікування, масаж, Бобат-терапія, Войта-терапія тощо). Основна група (53 пацієнта) на тлі загальноприйнятої комплексної терапії додатково отримувала курс ПНГ за допомогою індивідуального апарата гірського повітря типу «Борєй-М» (виробництва наукового медично-інженерного центру НОРТ НАН України, м. Київ). Для проведення ПНГ використовували нормобаричну газову гіпоксичну суміш (ГГС-12), яка складалась з 12 % кисню та 88 % азоту. Сеанси проводили один раз на добу в інтермітуючому режимі: 15 хв – дихання ГГС-12, 5 хв – атмосферним повітрям (один цикл). Кількість циклів збільшилася від одного до трьох. Курс ПНГ у середньому складав 10 сеансів. Після проведеного комплексного лікування відзначали позитивну динаміку стану рухового статусу у 94 % хворих основної (з використанням ПНГ) групи та у 74 % групи порівняння. Електроенцефалографічне дослідження пацієнтів обох груп виявило позитивні зміни у 70 % пацієнтів основної групи та у 56 % групи порівняння. Транскраніальна допплерографія судин головного мозку встановила наявність позитивної динаміки у 85 % дітей основної групи та у 59 % групи порівняння. При проведенні офтальмоскопічного дослідження позитивні зміни у стані очного дна відзначали у 32 % пацієнтів основної групи та у 12 % групи порівняння.

Ключові слова: дитячий церебральний параліч, переривчаста нормобарична гіпоксія, адаптація.

REFERENCES

1. Агаджанян А.Н., Миррахимов М.М. Горы и резистентность организма. – М.: Наука, 1970. – 182 с.
2. Березовский В.А. Аллопатический и гомеопатические принципы в лечении заболеваний, связанных с кислородным голоданием / Молекулярные аспекты адаптации к гипоксии. – К.: Изд-во Наук. думка, 1979. – С. 224–231.
3. Березовский В.А., Дейнега В.Г. Физиологические механизмы саногенных эффектов горного климата. – Там же, 1988. – 224 с.
4. Жирмунская Е.А. Система описания и классификация энцефалограмм человека. – М. Медицина, 1984. – 234 с.
5. Зайко М.Н., Биць Ю.В., Бутенко Г.М. Патофізіологія: підручник.– К.: Медицина, 2008. – 703 с.
6. Зенков Л.Р., Карлов В.А., Ронин М.А. Спектральный анализ ЭЭГ у детей и подростков, страдающих эпилепсией: общие характеристики и патофизиологическая интерпретация даннях / Журн. неврологии и психиатрии. – 1989. – 89, № 1. – С. 15–19.
7. Кравчук В.Є., Мартинюк В.Ю., Зінченко С.М. Допплеренцефалографія у дітей / Основи медико-соціальної ребілітації дітей з органічним ураженням нервової системи. – К.: Інтермед, 2005. – С. 140–146.
8. Лобов М.А. Коррекция мышечного тонуса и дизартрии при детском церебральном параличе / Журн. мед. консилиум («Consilium medicum»). – 2001. – 3, №14. – С. 34–38.
9. Семенова К.А. Методические рекомендации по применению рабочей классификации детского церебрального паралича. – М., 1973. – 20 с.
10. Березовський В.Я., Горбань Є.М., Левашов М.І., Сутковий А.Д. Методичні рекомендації Мінздраву України: Технологія підвищення резистентності організму за допомогою гіпокситерапії. – К., 2000. – 34 с.
11. Березовський В.Я., Яценко К.В. Методичні рекомендації Міністерства охорони здоров'я України: інструментальна оротерапія в комплексній реабілітації дітей з органічним ураженням нервової системи. – К., 2009. – 23 с.
12. Михайленко В.Е. Клинико-нейрофизиологическое обоснование применения физических факторов в реабилитации детей с ДЦП: автореф. дис. на присвоение науч. степени канд. мед. наук: спец. 14.03.04 «Патологическая физиология». – Ялта. – 2005. – 23 с.
13. Надоненко О.М., Мартинюк В.Ю., Зінченко С.М. Електроенцефалографічні характеристики у дітей від народження до 3-х років в стані сну і неспання / Основи медико-соціальної ребілітації дітей з органічним ураженням нервової системи. – К.: Інтермед, 2005. – С. 120–134.
14. Панасюк Л.О., Мартинюк В.Ю., Зінченко С.М.. Обстеження неврологічного статусу у новонароджених / Основи медико-соціальної ребілітації дітей з органічним ураженням нервової системи. – Там же. – С. 47–53.
15. Росин Ю. А. Допплерография сосудов головного мозга у детей. – С.-Петербургское мед. изд-во, 2004. – 110 с.
16. Сидоренко Е.И. Офтальмология. – М.: ГЭОТАР-МЕД, 2002. – 408 с.
17. Сіротинін М. М. Життя на висотах і хвороба висоти. – К.: Вид-во АН УССР, 1939. – 225 с.
18. Статистичний бюлетень: заклади охорони здоров'я та захворюваність населення України у 2007 р. / Держкомстат України. – К., 2008. – 96 с.
19. Осауленко О.Г. Статистичний щорічник України: за 2006 р. / Держкомстат України. – К.: Консультант, 2007. – 575 с.
20. Palisano R., Rosenbaum P., Bartlett D., Livingston M. Content validity of the Expanded and Revised Gross Motor Function Classification System / Developmental Medicine and Child Neurology. – 2007. – №9. – P. 57–68.

O.O.Bogomoletz Institute of Physiology, National Academy of Sciences of Ukraine, Kyiv

Received 02.12.2012