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EFFICIENCY OF NEUROMETABOLIC THERAPY AMONG THE PATIENTS WITH ISCHEMIC HEMISPHERIC STROKE IN RECOVERY PERIOD

Summary. Cerebrovascular diseases, and especially their acute forms, cerebral strokes, are an important problem in modern medicine. The search and usage of new and more effective drugs, which contribute to the improvement of treatment results in the recovery period of the disease, are relevant.

The aim of the study – to improve the treatment of patients with cerebral ischemic stroke in the recovery period by using phenylpiracetam in the complex therapy.

Materials and Methods. The work presents the results of treatment of 70 patients (average age is (58.8±0.9) years) in the recovery period of ischemic hemispheric stroke (IHS). All the patients were divided into two clinical groups of 35 patients. The group 1 included the patients who received phenylpiracetam in a complex therapy orally in a daily dose of 200 mg, divided into 2 intakes: in the morning and at lunch for 30 days; the group 2 consisted of patients who received piracetam as a nootropic drug parenterally in a daily dose of 3000 mg once in the morning during 30 days. All the patients were carried out in the dynamics before the treatment and after 30 days the assessment of the state according to the stroke scale of the National Institute of Health in order to determine the severity of the stroke. The degree of functional restoration according to Modified Rankin Scale and the estimation of the ability of household skills and self-service according to the Barthel Index were determined. A dynamic evaluation of cognitive impairments was performed using the Mini-Menthal State Examination and the 10-word memory test.

Results and Discussion. As a result of treatment, positive dynamics of all clinical-neurological and cognitive indicators was observed, it was more revealed in patients of the main group using phenylpiracetam, compared with the control group ($p<0.05$). In the main group, after the therapy, MMSE points increased by 13.0 % ($p<0.01$) due to the improvement of most cognitive domains: memory in 2 times ($p<0.01$), attention and calculation – by 33.3 % ($p<0.01$), orientation – by 12.5 % ($p<0.01$). In the control group it was registered statistically significant but less revealed, in comparison with the main group, the increasing of points according to MMSE (Δ% + 4.2 %, $p<0.01$).

Conclusions. The conducted research informs us about positive effects of the Phenylpiracetam drug, which contribute to the improvement of treatment outcome among the patients with IHS in the recovery period.

Key words: stroke; recovery period; rehabilitation.

INTRODUCTION Cerebrovascular diseases, and especially their acute forms, cerebral strokes, are an important problem in modern medicine [1, 2]. This is due to their significant prevalence, morbidity, mortality and invalidity of patients. In Ukraine, these indicators, unfortunately, exceed the average European ones. Annually in Ukraine, it is registered up to thousand brain strokes [3]. Of those who survived, the majority of patients, more than 80 %, remain disabled. Therefore, the problem is rather actual not only in medical but in socio-economic sphere as well [4, 5].

One of the priority directions in the fight against stroke is neuro-rehabilitation. Objectives and tasks of rehabilitation are to achieve the maximum possible recovery of patients [6]. At the stage of rehabilitation, complex therapy is being carried out, including the use of drugs. Therefore, the search and the usage of new and more effective drugs, which contribute to the improvement of the results of treatment, is relevant [7, 8, 9].

The aim of the study – to improve the treatment of patients with IHS in the recovery period through the use of Phenylpiracetam in the complex therapy.

MATERIALS AND METHODS There were 70 patients (44 men and 26 women) aged from 40 to 73 years (average age was (58.8±0.9) years) in the recovery period of ischemic hemispheric stroke (average duration of the disease was (2.0±0.2) months) under our observation. The first (main) clinical group involved 35 patients aged from 40 to 73 years (average age was (59.7±1.5) years). There were 23 men (65.7 % of observations) and 12 women (34.5 % of observations) and they received Phenylpiracetam orally in a daily dose of 200 mg in complex neurorehabilitation therapy, divided into 2 doses: in the morning and at lunch during 30 days. The combination of Phenylpiracetam and other nootropics was not used. The second (control) group consisted of 35 patients (21 men and 14 women) aged from 46 to 69 years (average age was (57.9±1.1) years) who received Piracetam parenterally as a nootropic drug in a daily dose of 3000 mg once in the morning within 30 days.

The division of patients into groups was conducted in accordance with the conditions of randomization, including the correct sample by age, sex, degree of severity of neurological deficiency and cognitive impairments**.**

The criteria for inclusion in the study were the following ones:

1) Men and women with confirmed ischemic hemispheric stroke in the recovery period of the disease at the age over 40 years according to clinical and computed tomographic study;

2) the presence of cognitive dysfunctions in the studied patients.

3) voluntary, signed by the patient himself, informed consent to participate in the study.

The study excluded those patients who had the following criteria:

1) acute cerebrovascular accident in history;

2) hemorrhagic transformation of brain infarction;

3) combined stroke;

4) ≥ 2 lesions;

5) revealed aphasic disorders, which complicate the evaluation of cognitive function.

6) somatic pathology in decompensated stage (uncontrolled hypertension, sub- and decompensated diabetes, severe liver and kidney disease, obesity of the 3rd and 4th levels);

7) oncological pathology;

8) psychopathological syndrome.

The average time period from the moment of acute cerebral ischemia in the studied group was (2.1±0.3) months, in the control group – (1.9±0.3) months.

Clinical and neurological examination was performed before the treatment and on the 30th day, which included the evaluation as for the following scales:

1) Objectivization of the state of patients by the scale of stroke of the National Institute of Health of the United States (NIHSS), which allowed to assess the severity of stroke;

2) the degree of functional recovery and disability in patients with CIHS was evaluated by the Modified Rankin Scale (mRS);

3) the assessment of household skills and self-service was investigated using the Bartel Index (BI);

4) it was verified the presence of cognitive impairments and evaluated its structure using the Mini-Mental State Examination (MMSE);

5) research of short-term memory was carried out using 10-words memorization test (A. R. Luria, 1973).

In order to evaluate the effectiveness of rehabilitation measures involving Phenylpiracetam (main group) and the control group of patients, receiving Piracetam, a re-study was conducted 30 days later.

RESULTS AND DISCUSSION In the studied patients of the clinical structure of the post-stroke states, motor disorders of different degree of severity in the absence of statistically significant intergroup differences were dominated (Table1).

Against the background of combined therapy with Phenylpiracetam, it was recorded a decrease in the level of neurological deficiency by NIHSS by 20.0 % ($p<0.01$) and an increase in self-service level as for BI by 5.3 % ($p<0.01$).

In the control group, the level of neurological deficits by NIHSS decreased by 16.7 % ($p<0.01$), self-service level for BI increased by 11.1 % ($p<0,01$). After the conducted therapy, the studied groups as for the levels of neurological deficiency, self-service and disability did not differ significantly (Table 2).

All patients had cognitive impairments of different degree of severity before the treatment. The initial level of cognitive dysfunction as for MMSE scale in 2 patients (2.8 %) was defined as mild cognitive impairments, in 33 (47.2 %) patients – moderate cognitive impairments, in 34 (48.6 %) patients – dementia of light severity and in 1 patient (1.4 %) – dementia of moderate severity. The structure of the severity of cognitive impairments in the studied groups of patients before the treatment is presented in Table 3.

Before the treatment, the studied groups of patients did not differ significantly in terms of the severity of cognitive impairments for MMSE significance (23 (23; 24) points in the main group versus 24 (23; 24.5) points in the control one, $p= 0.788$).

The initial structure of dysfunction of cognitive domains in the studied groups of patients is presented in Table 4.

In both groups, cognitive dysfunction was presented by a predominant impairment of attention and calculation, memory and, to a lesser extent, orientation and perceptual-gnostic sphere. Statistically significant intergroup differences in dysfunction of cognitive domains were not detected.

In the main group, after the conducted therapy, according to MMSE scale points increased by 13.0 % ($p<0.01$) due to the improvement of most cognitive domains: memory in 2 times ($p<0.01$), attention and calculation – by 33.3 % ($p<0.01$), orientation – by 12.5% ($p<0.01$).

In the control group statistically significant, but less fixed compared with the main group, the increasing of points by MMSE scale ($\Delta\% + 4.2\%$, $p<0.01$), was recorded due to the improvement of such cognitive domains as memory, attention and calculation, orientation.

At the end of therapy, intergroup differences based on the MMSE values and the following cognitive domains such as memory, attention and calculation are recorded (Tabl. 5).

The above data confirm the predominance of anti-amnestic orientation of the pharmacotherapeutic effect of the drug in the aspect of exposure to cognitive dysfunction.

The initial violation of short-term memory of different degree of severity was verified according to the 10-words memorization test (A. R. Luria, 1973) in patients in the main

Table 1. Comparative characteristics of the levels of neurological deficiency, self-service and disability in the studied groups of patients before the treatment (Me (Q1; Q3))

Indexes	Main group n=35	Control group, n=35	p
NIHSS, points	5.0 (4.0; 6.5)	6.0 (4.5; 7.0)	0.374
BI, points	95.0 (90.0; 100.0)	90.0 (85.0; 95.0)	0.07
mRS, points	2.0 (2.0; 3.0)	2.0 (2.0; 3.0)	0.657

Table 2. Comparative characteristics of levels of neurological deficiency, self-service and disability in the studied groups of patients after treatment (Me (Q1; Q3))

Indexes	Main group n=35	Control group, n=35	p
NIHSS, points	4.0 (4.0; 6.0)	5.0 (3.0; 7.0)	0.861
BI, points	100.0 (97.5; 100.0)	100.0 (95.0; 100.0)	0.116
mRS, points	2.0 (2.0; 2.0)	2,0 (2,0; 3,0)	0.469

Table 3. Structure of severity of cognitive impairments in the studied groups of patients before the treatment

Severity of cognitive impairments	Range of points for MMSE	Main group, n=35	Control group, n=35
Light cognitive impairment	26–27	2 (5.7 %)	0 (0 %)
Moderate cognitive impairment	24–25	15 (42.9 %)	18 (41.4 %)
Dementia of light degree	20–23	17 (48.6 %)	17 (48.6 %)
Dementia of moderate degree	11–19	1 (2.9 %)	0 (0 %)

Table 4. Output structure of dysfunction of cognitive domains in the studied groups of patients

Cognitive domains	Maximum values for MMSE	Main group, n=35	Control group, n=35	p
Orientation	10	8.0 (8.0; 9.0)	8,0 (8.0; 8.5)	0.744
Perception	3	3.0 (2.0; 3.0)	3,0 (2.0; 3.0)	0.843
Attention and calculation	5	3.0 (3,0; 4.0)	3.0 (2.0; 4.0)	0.583
Memory	3	1.0 (1.0; 2.0)	1.0 (1.0; 2.0)	0.491
Perceptually-gnostic sphere	9	8.0 (7.0; 9.0)	9.0 (7.5; 9.0)	0.232

Table 5. Comparative characteristics of dysfunction of cognitive domains in the studied groups of patients after the treatment

Cognitive domains	Maximum values for MMSE	Main group, n=35	Control group, n=35	p
Orientation	10	9.0 (9.0; 9.0)	9.0 (8.0; 9.0)	0.124
Perception	3	3.0 (3.0; 3.0)	3.0 (2.5; 3.0)	0.4
Attention and calculation	5	4.0 (3.0; 4.0)	3.0 (3.0; 4.0)	0.032
Memory	3	2.0 (2.0; 3.0)	2.0 (2.0; 2.0)	0.042
Perceptually-gnostic sphere	9	8.0 (8.0; 9.0)	9.0 (7.5; 9.0)	0.506

and control groups in the absence of statistically significant differences (30.0 (22.0; 35.0) words and 28.0 (23.5; 30.0) words, p=0.338).

After conducting complex therapy patients of the main group significantly differed by a higher value in the test for memorizing 10 words (respectively, 35.0 (30.0; 40.0) versus 30.0 (23.5; 30.0), p<0.01).

In the main group there was a reliable and more fixed, in comparison with the control group, improvement of the integral index of short-term memory (Δ% + 16.7 against Δ% + 7.1, p<0.01 for both groups) (Fig. 1).

The results of our complex clinical-neurophysiological research are cohered with the data of other authors. So, in the study of L.V. Bagir and co-authors (2006) it was shown that the use of N-carbamoyl-methyl-4-phenyl-2-pyrrolidone in patients with CIHS in the early recovery period of the disease contributes to the improvement of cognitive functions against the background of increased levels of mobility, self-service and household activity [10].

CONCLUSIONS 1. The use of Phenylpiracetam in complex rehabilitation therapy allowed to reduce the level of neurological deficiency by NIHSS scale by 20.0 % (p<0.01) and increase self-service BI level – by 5.3 % (p<0.01).

2. It was fixed an increase in the number of points by the MMSE scale by 13.0 % (p<0.01) due to the improvement of the majority of cognitive domains: memory, attention, calculation, orientation (p<0.01) on the background of the treatment with Phenylpiracetam.

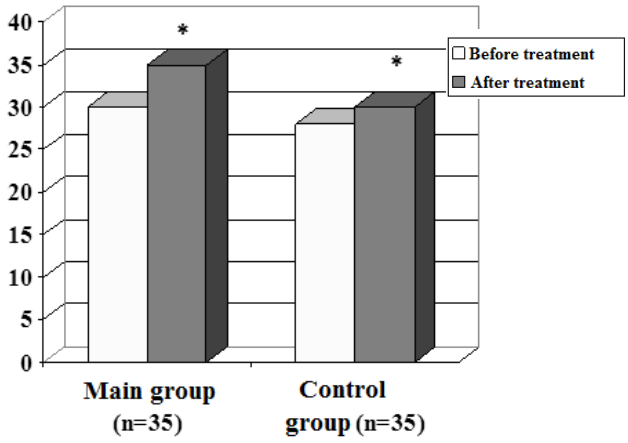

Fig. 1. Dynamics of short-term memory level of the test for memorizing 10 words in the studied groups of patients.

*Note: * – the reliability of the differences in the background of therapy p<0.01.*

The prospective of further research is study of influence of Phenylpiracetam on the dynamics of cognitive functions in the recovery period of ischemic hemispherical stroke.

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ЕФЕКТИВНІСТЬ НЕЙРОМЕТАБОЛІЧНОЇ ТЕРАПІЇ У ХВОРИХ НА ІШЕМІЧНИЙ ПІВКУЛЬОВИЙ ІНСУЛЬТ У ВІДНОВНОМУ ПЕРІОДІ

Резюме. Цереброваскулярні захворювання, особливо їх гострі форми, мозкові інсульти, є важливою проблемою у сучасній медицині. Пошук та застосування нових і більш ефективних препаратів, що сприяють поліпшенню результатів лікування у відновний період захворювання, є актуальними.

Мета дослідження – покращити лікування хворих на ішемічний мозковий інсульт у відновному періоді шляхом застосування в комплексній терапії препарату “Фенілпірацетам”.

Матеріали і методи. У дослідженні представлено результати лікування 70 хворих (середній вік (58,8±0,9) року) у відновному періоді ішемічного півкульового інсульту (ІПІ). Усіх пацієнтів поділили на дві клінічні групи по 35 осіб. Першу групу склали хворі, які в комплексній терапії отримували препарат“Фенілпірацетам” перорально в добовій дозі 200 мг, яку розділили на 2 прийоми, – вранці та в обід упродовж 30 днів, а другу – пацієнти, яким в якості ноотропного препарату отримували “Пірацетам” парентерально в добовій дозі 3000 мг одноразово вранці протягом 30 днів. Усім хворим в динаміці до лікування і через 30 днів проводили оцінку стану за шкалою інсульту Національного інституту здоров’я для визначення ступеня його тяжкості, зокрема функціонального відновлення за модифікованою шкалою Ренкіна й оцінку можливості побутових навичок і самообслуговування за індексом Бартела. Оцінювали динаміку когнітивних порушень із використанням Mini–Menthal State Examination та тесту запам’ятовування 10 слів.

Результати досліджень та їх обговорення. У результаті проведеного дослідження відзначали позитивну динаміку всіх клініко-неврологічних і когнітивних показників, вірогідно більш вираженою вона була у хворих основної групи, де застосовували препарат “Фенілпірацетам”, порівняно з групою контролю ($p<0,05$). В основній групі після проведеної терапії зареєстровано збільшення балів за MMSE на 13,0 % ($p<0,01$) за рахунок поліпшення більшості когнітивних доменів: пам’яті – в 2 рази ($p<0,01$), уваги та рахунку – на 33,3 % ($p<0,01$), орієнтації – на 12,5 % ($p<0,01$). У контрольній групі зареєстровано статистично значуще, але менш виражене, порівняно з основною групою, збільшення балів за MMSE (Δ %+4,2 %, $p<0,01$).

Висновки. Проведене дослідження свідчить про позитивні ефекти препарату “Фенілпірацетам”, що сприяють поліпшенню результатів лікування хворих на ішемічний півкульовий інсульт у відновному періоді.

Ключові слова: інсульт; відновний період; реабілітація.

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ЭФФЕКТИВНОСТЬ НЕЙРОМЕТАБОЛИЧЕСКОЙ ТЕРАПИИ У БОЛЬНЫХ ИШЕМИЧЕСКИМ ПОЛУШАРНЫМ ИНСУЛЬТОМ В ВОССТАНОВИТЕЛЬНОМ ПЕРИОДЕ

Резюме. Цереброваскулярные заболевания, особенно их острые формы, мозговые инсульты, являются важной проблемой в современной медицины. Поиск и применение новых и более эффективных препаратов, способствующих улучшению результатов лечения в восстановительный период заболевания, являются актуальными.

Цель исследования – улучшить лечение больных ишемическим мозговым инсультом в восстановительном периоде путем применения в комплексной терапии препарата “Фенилпирацетам”.

Материалы и методы. В исследовании представлены результаты лечения 70 больных (средний возраст (58,8±0,9) года) в восстановительном периоде ишемического полушарного инсульта (ИПИ). Всех пациентов разделили на две клинические группы по 35 лиц. Первую группу составили больные, которые в комплексной терапии получали препарат “Фенилпирацетам” перорально в суточной дозе 200 мг, разделенной на 2 приема, – утром и в обед в течение 30 дней, а вторую – больные, которые в качестве ноотропного препарата получали “Пирацетам” парентерально в суточной дозе 3000 мг однократно утром в течение 30 дней. Всем больным в динамике до лечения и через 30 дней проводили оценку состояния по шкале инсульта Национального института здоровья для определения степени его тяжести, особенно функционального восстановления по модифицированной шкале Рэнкина и оценку возможности бытовых навыков и самообслуживания по индексу Бартела. Оценивали динамичность когнитивных нарушений с использованием Mini–Menthal State Examination и теста запоминания 10 слов.

Результаты исследований и их обсуждение. В результате проведенного исследования отмечали положительную динамику всех клинико-неврологических и когнитивных показателей, достоверно более выраженой она была у больных основной группы, где применяли препарат “Фенилпирацетам”, по сравнению с группой контроля ($p<0,05$). В основной группе после проведенной терапии зарегистрировано увеличение баллов по MMSE на 13,0 % ($p<0,01$) за счет улучшения большинства когнитивных доменов: памяти – в 2 раза ($p<0,01$), внимания и счета – на 33,3 % ($p<0,01$), ориентации – на 12,5 % ($p<0,01$). В контрольной группе зарегистрировано статистически значимое, но менее выраженное, по сравнению с основной группой, увеличение баллов по MMSE (Δ%+4,2 %, $p<0,01$).

Выводы. Проведенное исследование свидетельствует о положительных эффектах препарата “Фенилпирацетам”, способствующие улучшению результатов лечения больных ишемическим полушарным инсультом в восстановительном периоде.

Ключевые слова: инсульт; восстановительный период; реабилитация.

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