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Use of the drug pantogam syrup in the treatment of affective-respiratory paroxysms in young children

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Purpose of the study. The effectiveness of the drug pantogam syrup10% (hopantenic acid) in the treatment of affective-respiratory attacks (ARA).**Material and methods.**A total of 60 children aged 2 to 4 years with ArP were examined. An assessment of clinical manifestations and neurophysiological examination data (long-term video-EEG monitoring) in children with paroxysms was carried out, and their anxiety level was determined. During the study, the children were divided into two groups: the main group (30 patients), where pantogam syrup was used as ArP therapy (100 mg/ml for 3 months at a dose of 30-35 mg/kg per day) and a comparison group (30 patients), in which the condition was corrected only by psychological methods.**Results and conclusion.**After the course of treatment, improvement was noted in 73.3% of patients in the main group compared to 16.7% in the comparison group. The indicators of the level of children's anxiety also significantly decreased after the neuroprotective therapy. A comparative analysis of electroencephalographic indicators revealed a reliable decrease in the power of slow-wave rhythms. The results obtained allow us to judge the high effectiveness of pantogam syrup in the treatment of children with this pathology.

Key words: affective-respiratory attack, pantogam syrup.

The use of Pantogam syrup in treating small children's breath holding spells

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Objective. to study the efficacy of pantogam syrup 10% (hopantenic acid) in the treatment of breath-holding spells (BhS).**Materials and methods**. Sixty children, aged from 2 to 4 years, with BhS were studied. the evaluation of clinical manifestations and anxiety level was performed. results of neurophysiological examination (long-term video-eeG-monitoring) were analyzed. children were divided into 2 groups: main, in which the patients received pantogam syrup, and control group, in which only psychological methods were used. **Results and Conclusion**. the results of the clinical and neurophysiological studies performed after the treatment, showed the clinical improvement in 73.3% of patients of the main group compared with similar data from the children in the control group (16.7%). the anxiety level decreased significantly after the neuroprotective therapy. A comparative analysis of electroencephalographic indicators demonstrated a significant (r<0.05) reduction in the power range of slow rhythms and manifestations of functional immaturity of the brain in patients of the main group. these results provide evidence for the high efficacy of pantogam syrup in the treatment of children with BhS.

Keywords: breath-holding spells, Pantogam-syrup.

Affective-respiratory attacks (ARP) are episodic occurrences of apnea in children, often accompanied by loss of consciousness, impaired muscle tone and convulsions as a response to negative emotions that they cannot control. The frequency of ARP in the child population, according to various authors, ranges from 4 to 17% [1-3]. Attacks usually appear at the end of the first year of life and can continue until 3-4 years of age, and are less common up to 5 years.

The term “breathholding spells” is often used to describe these paroxysms, but it is not entirely appropriate, since it implies a voluntary nature of breathing and does not reflect the involuntary nature of the occurrence of ARP [4, 5].

The manifestation of paroxysms is noted at the age of 6-12 months [1, 2, 4], less often - at 2-3 years, and the end of attacks occurs at the age of 4-5 years, however, cases of ARP occurrence have been described both in infants aged 3 days [6] and in children aged 8 and even 10 years [7]. The frequency of attacks varies from several times a year to multiple during the day. Most researchers agree that ARP are provoked paroxysms, the implementation of which requires the influence of exogenous factors that cause negative emotions in the child (parents' "disobedience", inability to achieve what is desired or to attract attention, etc.) [1, 5, 8].

As a reaction to provoking factors, there is intense crying with hyperventilation of the lungs and subsequent hypocapnic ischemia of the brain, a decrease in arterial pressure. The child takes a deep breath, a reflex spasm of the muscles of the larynx and bronchi occurs, leading to apnea, hypoxemia and, as a consequence, hypoxemia.

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hypoxia of the brain (the Valsalva-Weber mechanism is activated: as a result of increased intrathoracic pressure, venous return to the heart decreases, cardiac output decreases, which leads to hypoperfusion of the cerebral arteries). This is followed by inhalation, restoration of breathing and consciousness, short-term muscle hypotension (much less often - generalized tonic muscle tension as a result of severe hypoxia of the brain during apnea) and subsequent lethargy, sometimes sleep. The attack lasts 30-60 seconds, while cyanosis of the skin of varying severity is noted - from involvement of the nasolabial triangle to diffuse (the so-called "blue", "cyanotic" paroxysm). "The child is in stitches" - this is how his parents describe this condition. But sometimes, which often happens with fright or sudden pain (hit, pricked), cyanosis is not very pronounced, pallor is noted, asystole lasting up to 10-15 s occurs, a so-called "pale" attack occurs. Thus, the main pathogenetic link in ARP is apnea or a combination of apnea and asystole [1, 2, 9], as a result of which many authors [4, 10-12] consider these paroxysms in the structure of life-threatening conditions.

The aim of this study is to investigate the effectiveness of using the drug pantogam syrup 10% (hopantenic acid) in the treatment of ARP.

Pantogam (hopantenic acid) in its chemical structure is a calcium salt of D(+)-pantoyl-γ-aminobutyric acid and is the highest homologue of D(+)-pantothenic acid, in which β-alanine is replaced by γ-aminobutyric acid, GABA, which is one of the main inhibitory mediators of the central nervous system. Homopantothenic acid is a natural metabolite of GABA in the nervous tissue. It penetrates the blood-brain barrier, practically not being metabolized in the body, and has a pronounced effect on the functional activity of the central nervous system: it helps to improve GABAergic neurotransmitter transmission, thereby enhancing the control function of the cerebral cortex over the subcortical structures; increases the brain's resistance to hypoxia and the effects of toxic substances; stimulates anabolic processes in neurons; combines a moderate sedative effect with a mild stimulating effect; reduces motor excitability; activates mental and physical performance [10].

Material and methods

We observed 60 children suffering from ARP, aged 2 to 4 years, 33 (55.0%) boys and 27 (45.0%) girls (mean age 3.2±0.8 years). The examined children were divided into two groups. In the main group (30 children), pantogam syrup 100 mg/ml (hopantenic acid) was used to correct neurological deficit for 3 months at a dose of 30-35 mg/kg per day. The comparison group included 30 children diagnosed with ARP, whose parents did not want to carry out drug treatment for their children, limiting themselves to the recommendations of a clinical psychologist. The exclusion criteria from the study were the age of children under 2 and over 4 years, the presence of gross focal neurological symptoms, severe somatic pathology, epilepsy, history of static seizures confirmed by EEG studies, mental retardation, taking medications that affect the central nervous system.

The conducted examination included collecting complaints from parents, studying the clinical history and assessing the manifestations of affective-respiratory paroxysms, recording objective examination data - assessing the somatic and psychoneurological status according to the generally accepted scheme [14]. In addition, EEG (long-term video-EEG monitoring) was carried out using a 21-channel electroencephalograph Neuron-Spectrum-4/P Neurosoft. The general functional state of the brain, the level of maturation of the brain's bioelectrical activity, the presence of local changes in biopotentials, the level of formation of cortical-subcortical connections were assessed, and the spectral power of the main rhythms between groups of subjects in the theta (4-7 Hz), alpha (8-13 Hz), beta (14-20 Hz), beta (20-30 Hz) ranges was analyzed.

Parents were required to keep a detailed diary for 90 days from the start of the study, indicating the recurrence of ARP in the child, a description of their clinical picture, the provoking factor and the duration of the paroxysm.

In order to identify the level of children's anxiety, we used the questionnaire of G.P. Lavrentyeva, T.M. Titarenko "Level of Child Anxiety" (1992), consisting of 20 statements characterizing the child's behavior, as well as the anxiety test (R. Tamml, V. Amen, M. Dorki), assessing the situational emotional experience of the child, with subsequent calculation of the anxiety index. The child's condition was assessed on the eve of the start of the study (day 0) and at the end of the study (day 90).

Hypotheses about the difference between group arithmetic means were tested using two-sided *t*-Student's t-tests for related or unrelated populations.

Research results

After the course of therapy with Pantogam syrup, clinical improvement was achieved in 22 (73.3%) children — ARPs did not recur or were isolated. In 8 (26.7%) children from this group, ARPs continued to be observed. Other adverse effects and complications were not observed. In the comparison group, clinical improvement or complete disappearance of ARPs was noted in 5 (16.7%) children, while in 25 (83.3%) children, ARPs recurred, and their clinical expression did not differ from the initial level before the start of the study.

Evaluation of the condition after a course of treatment with pantogam showed a significant decrease in anxiety in children of the main group.**(see table)**. No significant change in anxiety levels was observed in the comparison group.

When comparing the EEG results before and after the course of pantogam use, the following positive changes were noted: a statistically significant increase in alpha activity in the parietal-occipital leads of both hemispheres of the brain ($r<0.005$), a decrease in the representation of beta and beta activity in the fronto-central-temporal leads ($r<0.05$), as well as a decrease in the power of the theta and delta range waves in all leads ($r<0.05$ and $r<0.005$, respectively). Many children noted

Results of anxiety assessment in the study groups

Group	Days of examination	Anxiety indicators
Main group (*n*=30)	0th	65.69±5.08
	90th	47.51±5.89*#
Comparison group (*n*=30)	0th	66.19±4.73
	90th	62.84±5.51

*Note.** - statistically significant difference before and after treatment (*r*<0.05);# — statistically significant difference between the main group and the comparison group (*r*<0.05).

an increase in the peak frequency in the theta range began. The appearance of epileptiform activity after the course of pantogam was not observed. In children from the comparison group, no significant EEG changes were noted (*r*>0.05).

Conclusion

The results obtained during the present study indicate clinical improvement in the condition of reduction of anxiety and the power of slow-wave range waves (delta, theta) of EEG and a decrease in the manifestations of functional immaturity of the brain in patients of the main group. These results indicate the activation of neurometabolic processes when using pantogam. The presence of a pronounced clinical effect and the safety of its use allow us to recommend pantogam syrup as the drug of choice in the treatment of ARP.

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