Prior to the study 807 patients were in monotherapy (62%), 468 patients were on 2 drugs (36%), 26 patients received 3 anticonvulsants (2%).

In the treatment with carbamazepine and oxcarbazepine complete clinical remission was achieved in 151 patients (44%), in 191patients (56%) treatment had no effect.

Upon receiving lamotrigine complete clinical remission was achieved in 51% of patients, in 49% patients there was no effect.

Upon receipt of topiramate complete clinical remission was achieved in 197 patients (61%), 125 (39%) patients remained resistant to topiramate therapy.

When treated with valproate 225 patients (71%) showed complete clinical remission, 90 patients (29%) were therapy resistant.

In levetiracetam treatment clinical remission was achieved in 160 patients (71%), in 66 patients (29%) pharmacological resistance was observed.

In 45% of patients who received two (39%) or more AED (6%), the efficiency of treatment was lower than in the monotherapy group. Clinical remission (with good drug tolerance and retention on therapy) was achieved in 27.5% of patients, reduction in the number of seizures to less than 50% was achieved in 28.9% of patients, lack of treatment effect was observed in 43.6% of patients.

In duotherapy the most effective combinations were levetiracetam + valproate, topiramate + valproate.

In polytherapy, the most effective combinations were oxcarbazepine + levetiracetam + valproate and levetiracetam + valproate +topiramate.

Conclusion. The most effective medication in the age group 1-6 years were levetiracetam and valproate, in the age group 7-14 years – topiramate and valproate, in the age group 15-17 years — lamotrigine and levetiracetam. For the prognosis of the course and efficiency of therapy, the etiology of epilepsy and the age of debut are essential. Exogenous factors such as chronic persistent infections, traumatic brain injury, somatic and infectious diseases can worsen the course and reduce the efficiency of treatment.

Key words: children, epilepsy, treatment efficacy.

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THE HOLTER ELECTROCARDIOGRAM MONITORING METHOD FOR EVALUATING THE HEART RHYTHM VARIABILITY IN CHILDREN WITH DIABETES MELLITUS OF TYPE 1

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Introduction. The study of close relationship between the state of the vegetative nervous system (VNS) and the cardiovascular system is still actual [1,2]. The heart, as you know, has its own automatism. The sine node is the main driver of the rhythm, which is controlled by two vegetative nerves, and the type of interaction between them is called functional synergism, that is, when the degree of activity of one of the departments changes, the effect of the other will be the opposite [3,4,5]. The imbalance of the VNS leads to a violation of the physiological regulation in the child's body, which may also have an effect on the function of the conduction system of the heart, but the effect of the VNS on the cardian rhythm is modulatory rather than controlling [6]. It was shown earlier that the greater the vagal effect of the heart is, the better adaptive capabilities are [7,8,9]. One of the informative methods that can reveal the predominant influence of this or that department on the heart rhythm is the heart rate variability (HRV) according to the Holter monitoring of the electrocardiogram (ECG) [10,11,12].

Aim. To study the state of vegetative regulation (VR) according to the results of HRV in children with type 1 diabetes mellitus (DM) during the Holter ECG monitoring on a daily basis.

Object and methods of research. Under supervision, there were 40 children aged 2.5 to 16 years old, of which 20 children with DM (the first one was the main group) and 20 children without DM (the second group) who underwent the Holter ECG monitoring while in the Department of Endocrinology of the Children's Municipal Clinical Hospital in Poltava. The number of both boys and girls in both groups was the same (11 and 9 respectively). The children of both groups, depending on their age, were divided into two subgroups of 10 children in each subgroup: the first subgroup of the main group consisted of the children under the age of 10, the second subgroup of the main group − children from 11 to 16 years old. A similar distribution of children was in the second group of children without DM.

The state of all the examined children of the main group was considered difficult; all children were hospitalized in a state of ketoacidosis.

The main method of research, in addition to the clinical and laboratory examination, was the Holter monitoring of the ECG on a daily basis, carried out on the device "CARDIOSENS K" (National Aerospace University "KhAI" and STC of electronic medical devices and technologies "KhAI-MEDICA", Kharkiv). Three ECG channels

Table 1.

Heart rate variability time rates for examined children with type 1 diabetes, according to the Holter electrocardiogram monitoring (M ± m)

Time Parameters of HRV	Keeping awake				Sleeping			
	I group (n = 20)		II group (n = 20)		I group (n = 20)		II group (n = 20)	
	1 sub-group (n = 10)	2 sub-group (n = 10)	1 sub-group (n = 10)	2 sub-group (n = 10)	1 sub-group (n = 10)	2 sub-group (n = 10)	1 sub-group (n = 10)	2 sub-group (n = 10)
avNN (мs)	611,71 ±16,8 p	692,0 ±17,3 < 0,05	525,7 ±14,4 p<	641,5 ±18,4 0,001	830,2 ±20,3 p	941,5 ±17,3 < 0,01	736,3 ±15,3 p <	836,7 ±14,8 0,002
SDNN (мs)	64,88 ±7,0 p	87,91 ±7,9 < 0,01	51,73 ±4,71 p	74,32 ±6,82 < 0,01	100,87 ±7,44	111,1 ±8,23	79,86 ±6,37	98,33 ±8,33
rMSSD (мs)	54,28 ±5,20	60,62 ±5,37	35,22 ±3,03 p	56,11 ±4,87 < 0,02	112,57 ±6,36	110,0 ±7,31	79,66 ±6,84	91,44 ±6,81

Note: n – the number of children in the group.

with the system of assignments – AVFmod, V2mod, V5mod – were registered.

For evaluation of the state of VNS under the Holter ECG monitoring, there was performed time and spectral (frequency) analysis of daily recording in 5-minute intervals of the ECG. When evaluating short-term HRV, the spectral or frequence domain is more frequently used, while during a day the most informative is the time domain.

The main time characteristics of the HRV were investigated. avNN (ms) – the average value of all RR intervals – shows the basic level of sine node functioning and correlates with the heart rate parameter. SDNN (ms) – the standard mean square deviation of all RR intervals – is the integral index, which mainly reflects the total impact effect on the sine node of the sympathetic and parasympathetic VNS units and characterizes the HRV as a whole. rMSSD (ms) – the mean square deviation of the difference between successive RR intervals – reflects the ability of the sine node to concentrate the heart rate, the marker of activity of the parasympathetic VNS link. In the spectral analysis of HRV, the following parameters were calculated: high frequency, low frequency, and very low frequency. High frequency oscillations are fluctuations of the heart rhythm at a frequency of 0.15-0.40 Hz. Low frequency oscillations are part of the spectrum in the frequency range of 0.04-0.15 Hz. Very low frequency oscillations are the frequency range of 0.0033-0.04 Hz.

Statistical processing was performed using the Microsoft Excel 7.0 statistical software package with an average count (M) and a standard deviation (m). Indicators studied were compared among themselves within the group. Evaluation of differences in the studied groups of patients was performed on the basis of parametric criteria of the Student t-criterion; the differences were considered to be reliable at p <0.05. A correlation analysis (Spirman correlation coefficient) was used to detect the correlation of rhythm indices. Reliable values were taken at the significance level of 95% (p <0.05).

Results of the research and their discussion. In order to detect violations of HRV in children with DM, an analysis of the daily HRV was performed in both of the examined groups.

The results of the analysis of HRV time rates in the examined children according to the Holter monitoring of ECG are presented in **table 1.**

A significant increase in HRV time rates, which reflects the baseline level of sine node functioning (avNN, SDNN) in children with DM in both subgroups during sleep, compared with those during wakefulness, indicates the precondition for the formation of circadian rhythms of heart rate. According to the data obtained, in children with DM of both subgroups during wakefulness and sleep, the temporal rMSSD, which reflects the heart rate function, was unreliable over time compared with the temporal indices of children without DM, which characterizes instability of cardiac rhythm in the form of sine arrhythmias, and also explains long pauses of the rhythm due to episodes of sinoarthritic blockade.

Spectral analysis data are presented in **table 2.**

In the analysis of indicators of the spectral characteristics of HRV in children with DM, in particular HF (high-frequency component), which reflects the level of parasympathetic effects in cardiac rhythm regulation, the LF (low-frequency component), which characterizes the state of the sympathetic department of the vegetative nervous system, the system of regulation of vascular tone, it was established, that oscillations of the indicator of the sympathetic department of the VNS (LF) in children with DM and the group of children without DM were divergent during the day. Consequently, the data we have received indicate the existing autonomic imbalance in children with DM overnight, regardless of sleep or wakefulness of the children. It should be emphasized that low-frequency oscillations characterize not only the state of the sympathetic department of the VNS, but also reflect the activity of the subcortical vasomotor center.

It is known that an increase in VLF LF (very low-frequency component), indicates the activation of higher vegetative centers, since the amplitude of VLF is closely related to the psycho-emotional inhomogeneity and functional state of the cerebral cortex [3]. The VLF indicator reflects cerebral ergotropic effects at below levels and allows us to form an oppinion about the functional state of the brain in psychogenic and organic pathology of the brain [10]. An increase in the VLF component in children with DM, a marker of cerebral ergotropic activation, confirms the presence of chronic stress in children with DM. With organic lesions of the brain, VLF component is reduced [11,12].

The data we have received coincide with common opinion about the difficulties of unambiguous interpretation of the data of the HRV analysis and information

Table 2.

Spectral characteristics of heart rate variability in examined children with type 1 diabetes, according to the Holter monitoring of electrocardiogram (M ± m)

Para-meters of HRV Frequency	Keeping awake				Sleeping			
	I group (n = 20)		II group (n = 20)		I group n = 20)		II group (n = 20)	
	1 subgroup (n = 10)	2 subgroup (n = 10)	1 subgroup (n = 10)	2 subgroup (n = 10)	1 subgroup (n = 10)	2 subgroup (n = 10)	1 subgroup (n = 10)	2 subgroup (n = 10)
VLF (мс^2)	1083,71 ±107,1 p	2282,0 ±174,2 < 0,001	944,33 ±90,8 p	1900,77 ±164,0 < 0,001	1445,42 ±114,2 p	2836,5 ±234,0 < 0,001	1582,88 ±118,1 p<	2603,0 ±214.4 0,001
LF (мс^2)	986,43 ±101,3	1905,75 ±163,1	707,0 ±72,8 p	1352,44 ±147,0 < 0,001	2271,1 ±144,3	2730,75 ±201,0	1700,22 ±127,1 p<	2414,11 ±227,1 0,001
HF (мс^2)	1578,57 ±140,1	1841,37 ±184,4	826,66 ±84,5	1111,77 ±123,1	5983,85 ±513,1	5600,75 ±511,1	3068,66 ±219,1	3581,88 ±311,2

Note: n – the number of children in the group.

about the lack of correlation between the parameters of frequency and spectral analysis. Comparison of the obtained results indicates that both departments of the VNS are interested in the formation of violations of HRV in children with DM.

The use of the Holter ECG monitoring contributed to the detection of electrical instability of the myocardium in 55% of children in the primary group with DM (25% in each subgroup). The detected increase in dispersion (according to the standard ECG) and the variability (according to the Holter ECG monitoring) of the QT interval in patients with DM in the form of an elongated and slightly elongated compared with the age-sexual norm of the QT interval allows to timely form risk groups for children, which have a risk of developing arrhythmias. In the group of children without DM, the electrical instability of the myocardium was less pronounced.

Conclusions

1. Evaluation of heart rate variability according to the Holter ECG monitoring is an important informative indicator that allows timely formation of risk groups for children at risk of developing arrhythmias.

2. Identified risk groups for children at risk of developing arrhythmias, based on the Holter monitoring of ECG, require this survey to be conducted in dynamics.

3. The data of spectral characteristics of HRV (VLF, LF) testify to the high voltage of vegetative-regulatory mechanisms under the conditions of chronic stress in children with type 1 diabetes mellitus.

4. Conducting the Holter monitoring of ECG in children with type 1 diabetes mellitus showed that two departments of the VNS are involved in the formation of violations of heartbeat autonomic regulation.

Prospects for further research. It is planned to study neuropsychiatric development and morbidity of children with diabetes type 1 in the Poltava region.

The authors state that there is no conflict of interest in this article.

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МЕТОД ХОЛТЕРІВСЬКОГО МОНІТОРУВАННЯ ЕКГ В ОЦІНЦІ ВАРІАБЕЛЬНОСТІ СЕРЦЕВОГО РИТМУ У ДІТЕЙ З ЦУКРОВИМ ДІАБЕТОМ 1-ГО ТИПУ

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Резюме. *Мета:* вивчити стан вегетативної регуляції (ВР) за результатами варіабельності серцевого ритму у дітей з цукровим діабетом 1-го типу під час добового Холтер-моніторування ЕКГ.

Об'єкт і методи дослідження. Під наглядом знаходилось 40 дітей у віці від 2,5 до 16 років, з них 20 дітей з цукровим діабетом 1-го типу (перша – основна група) та 20 дітей без цукрового діабету (друга група), яким

проводилося Холтерівське моніторування ЕКГ під час знаходження у відділенні ендокринології Дитячої міської клінічної лікарні м. Полтава. Діти обох груп в залежності від віку були розділені на дві підгрупи по 10 дітей в кожній підгрупі: перша підгрупа основної групи – діти у віці до 10 років, друга підгрупа основної групи – діти від 11 до 16 років. Аналогічний розподіл дітей був в другій групі дітей без ЦД.

Результати. Проведення Холтерівського моніторування ЕКГ у дітей з ЦД показало, що у формуванні порушень вегетативної регуляції серцевого ритму задіяні обидва відділи ВНС. Дані спектральних характеристик ВСР (VLF, LF) свідчать про вагому напругу вегетативно-регуляторних механізмів в умовах хронічного стресу у дітей з ЦД 1-го типу.

Застосування Холтерівського моніторування ЕКГ сприяло виявленню електричної нестабільності міокарду у 55% дітей основної групи з ЦД (по 25% в кожній підгрупі). Виявлене збільшення дисперсії (за даними стандартної ЕКГ) і варіабельності (за даними Холтерівського моніторингу ЕКГ) інтервалу QT у хворих з ЦД 1-го типу у вигляді подовженого і дещо подовженого в порівнянні з віко-статевою нормою інтервалу QT дозволяє своєчасно сформувати групи ризику дітей, які мають загрозу розвитку аритмій.

Висновки. Виявлені групи ризику дітей, які мають загрозу розвитку аритмій, за результатами Холтерівського моніторування ЕКГ, потребують проведення даного обстеження в динаміці.

Ключові слова: діти, цукровий діабет, Холтерівське моніторування ЕКГ, аритмії.

МЕТОД ХОЛТЕРОВСКОГО МОНИТОРИРОВАНИЯ ЭКГ В ОЦЕНКЕ ВАРИАБЕЛЬНОСТИ СЕРДЕЧНОГО РИТМА У ДЕТЕЙ С САХАРНЫМ ДИАБЕТОМ 1-ГО ТИПА

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Резюме. *Цель:* изучить состояние вегетативной регуляции (ВР) по результатам вариабельности сердечного ритма у детей с сахарным диабетом 1-го типа во время суточного Холтер-мониторирования ЭКГ.

Объект и методы исследования. Под наблюдением находилось 40 детей в возрасте от 2,5 до 16 лет, из них 20 детей с сахарным диабетом 1-го типа (первая — основная группа) и 20 детей без сахарного диабета (вторая группа), которым проводилось Холтеровское мониторирование ЭКГ во время нахождения в отделении эндокринологии Детской городской клинической больницы г. Полтава. Дети обеих групп в зависимости от возраста были разделены на две подгруппы по 10 детей в каждой подгруппе: первая подгруппа основной группы — дети в возрасте до 10 лет, вторая подгруппа основной группы — дети от 11 до 16 лет. Аналогичное распределение детей был во второй группе детей без СД.

Результаты. Проведение мониторирования ЭКГ у детей с СД показало, что в формировании нарушений вегетативной регуляции сердечного ритма задействованы оба отдела ВНС. Данные спектральных характеристик ВСР (VLF, LF) свидетельствуют о весомую напряжение вегетативно-регуляторных механизмов в условиях хронического стресса у детей с СД 1-го типа.

Применение мониторирования ЭКГ способствовало выявлению электрической нестабильности миокарда у 55% детей основной группы с СД (по 25% в каждой подгруппе). Обнаружено увеличение дисперсии (по данным стандартной ЭКГ) и вариабельности (по данным Холтеровского мониторинга ЭКГ) интервала QT у больных с СД 1-го типа в виде удлиненного и несколько удлиненного по сравнению с веко-половой нормой интервала QT позволяет своевременно сформировать группы риска детей, представляющих опасность развития аритмий.

Выводы. Выявлены группы риска детей, представляющих угрозу развития аритмий, по результатам холтеровского мониторирования ЭКГ, требуют проведения данного обследования в динамике.

Ключевые слова: дети, сахарный диабет, Холтеровское мониторирование ЭКГ, аритмии.

THE HOLTER ELECTROCARDIOGRAM MONITORING METHOD FOR EVALUATING THE HEART RHYTHM VARIABILITY IN CHILDREN WITH DIABETES MELLITUS OF TYPE 1

Fesenko M. Ye., Fastovets M. M., Pokhylko V. I., Ovdiyenko O. D., Cherevko I. G.

Abstract. *Aim.* To study the state of vegetative regulation according to the results of heart rate variability in children with type 1 diabetes mellitus during the Holter electrocardiogram monitoring on a daily basis.

Object and methods of research. Under supervision were 40 children aged 2.5 to 16 years old, including 20 children with type 1 diabetes (the first – the main group) and 20 children without diabetes (second group) who underwent Holter monitoring of electrocardiogram during being in the Department of Endocrinology of the Children's Municipal Clinical Hospital in Poltava. Children of both groups, depending on their age, were divided into two subgroups of 10 children in each subgroup: the first subgroup of the main group – children under the age of 10, the second subgroup of the main group – children from 11 to 16 years old. A similar distribution of children was in the second group of children without diabetes.

Results. Conducting the Holter monitoring of ECG in children with diabetes showed that two departments of the vegetative nervous system are involved in the formation of violations of vegetative regulation of cardiac rhythm. The data of spectral characteristics of heart rate variability (VLF, LF) testify to the high voltage of vegetative-regulatory mechanisms under the conditions of chronic stress in children with type 1 diabetes.

The use of the Holter ECG monitoring contributed to the detection of electrical instability of the myocardium in 55% of children in the primary group with diabetes (25% in each subgroup). The detected increase in dispersion (according to the standard ECG) and the variability (according to the Holter ECG monitoring) of the QT interval in patients with type 1 diabetes in the form of an elongated and slightly elongated compared with the age-sexual norm of the QT interval allows to timely form risk groups for children, which have a risk of developing arrhythmias.

Conclusions. Identified risk groups for children at risk of developing arrhythmias, based on the Holter monitoring of ECG, require this survey to be conducted in dynamics.

Key words: children, diabetes mellitus, the Holter ECG monitoring, arrhythmias.

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