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SPECTRUM AND CHARACTERISTICS OF THE ELECTROCARDIOGRAPHIC CHANGES IN CHILDREN WITH TYPE I DIABETES MELLITUS

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Summary

Introduction. Type I diabetes mellitus (T1D) is one of the most widespread and socially significant diseases. Well-known as a co-occurring condition with youth-onset type 1 diabetes mellitus, cardiovascular disease manifests early after initial diagnosis as signs of cardiovascular remodeling. Growing data indicates that type 1 diabetic children and young adults experience subclinical heart dysfunction, central aortic stiffening, and accelerated peripheral vascular disease. Increased morbidity and mortality in adults have been linked to peripheral artery, heart, and cerebrovascular diseases, and early vascular alterations have been demonstrated to exist since childhood. Little is known to date concerning the development of early cardiac structural and functional problems in children with T1D. Early diagnostic is of high importance.

Aim. To assess the frequency and spectrum of electrocardiography (ECG) abnormalities in children with type 1 diabetes.

Materials and methods. Records of 60 patients with type I diabetes included into the analysis. ECG data, main anamnestic, clinical and laboratory data analyzed.

Results. So-called «small ECG abnormalities» were found. Incomplete left/right blockade bundle branch block found in 22.5 % of children, shortened PQ interval in 15 %, extrasystoles, tachycardia, bradycardia in 52.5 %, T wave amplitude decrease in 60 %. 87.5 % of the examinees have a combination of 2-3 of the above changes on the ECG. Only 12 % of the examined children had an ECG without pathological changes. All children with newly diagnosed type 1 DM had at least 1 of the described ECG abnormalities. Correlation analysis done. Substantial positive correlations between Hb1Ac levels and number of ECG changes, serum cholesterol levels and number of ECG changes were found.

Conclusions. The results of the study indicate that the majority of children with type I diabetes have so-called «small ECG abnormalities.» According to the type of disturbances, they can be classified as rhythm and conduction disturbances and combined changes. These findings are promising in terms of management tactics for children with type I diabetes, early detection and timely therapeutic correction of ECG abnormalities.

Keywords: type I diabetes, ECG, children, disorders, cardiovascular system

INTRODUCTION

Type I diabetes mellitus (T1D) is one of the most widespread and socially significant diseases. In various countries of the world, the number of patients with diabetes is 4-7 % of the population [1]. Epidemiological studies of diabetes in Ukraine are disappointing and indicate a constant increase in the number of patients [2]. One of the most serious complications of diabetes is

damage to the cardiovascular system, which is the main cause of death in patients with the type 1 diabetes.

The main cause of death for those with type 1 diabetes, cardiovascular disease (CVD), is known to be more common and more frequently related with T1D. But not every patient with type 1 diabetes has an increased risk of cardiovascular disease (CVD); this depends on the patient's unique characteristics and risk profile. To

better identify patients with type 1 diabetes who are at a higher risk, we must identify these predictive traits and risk markers [3].

The noninvasive method most frequently used for cardiac research is electrocardiography (ECG). Recent research has demonstrated that the course of type 1 diabetes is frequently accompanied by the development of new ECG abnormalities; in the Diabetes Control and Complications Trial (DCCT)/Epidemiology of Diabetes Interventions and Complications (EDIC) study, approximately three out of every four participants experienced at least one new ECG abnormality, and during the 16 years of follow-up in EDIC, approximately one out of every six experienced at least one new major ECG abnormality [4]. Furthermore, the presence of ECG indicators of myocardial ischemia in patients with type 1 diabetes was predictive of the development of coronary heart disease in the future, according to a small study with a brief follow-up. However, not fully studied the condition of ECG changes in children with T1D especially during the early stages of disease [4, 5].

AIM

The goal of the study was to assess the frequency and spectrum of ECG abnormalities in children with type 1 diabetes, to determine the main classes of abnormalities and their dependence of main metabolic markers in T1D.

MATERIALS AND METHODS

Patients data

Records of 60 patients with type I diabetes were included in the analysis. ECG data, main anamnestic, clinical and laboratory data analyzed. ECG tracings were

centrally read at hospital facility where patients were either treated examined during regular follow-ups. Initially, patients involved in the study underwent 12-derivation electrocardiography at a speed of 25 mm/h (Philips 2008 Seattle, WA, USA). Minor ECG abnormalities included minor isolated Q/QS-wave abnormalities, minor isolated ST/T abnormalities, high R waves/increased QRS voltage denoting left or right ventricular hypertrophy without strain pattern, nonischemic ST segment elevation, incomplete (left or right) bundle branch block, short PQ interval, extracyctoles, tachycardia and bradycardia were analyzed. Any ECG abnormalities (at least 1 mild ECG abnormality) that occur during the hospital stay or routine follow-up are the main focus of this analysis.

Statistics

The Shapiro-Wilk test was used for analysis if the data were compatible with the normal distribution in the statistical analyses. The results of the study are presented as mean±SEM. Data were analyzed using the Mann-Whitney test if the distribution of variables was nonparametric. Pearson correlation used to study the correlation between factors. Statistical data processing was performed using the software Past4 for Windows. A p value of <0,05 considered statistically different.

RESULTS

Basic clinical characteristics of patients

Sixty children with type I diabetes were examined. The gender distribution was as follows – 29 (45 %) boys and 31 (52 %) girls (figure 1A). Among them, 31 (52 %) with an average duration of the disease of 5.98±0.62 years, 29 (48 %) children had type I diabetes detected for the first time (figure 1B).

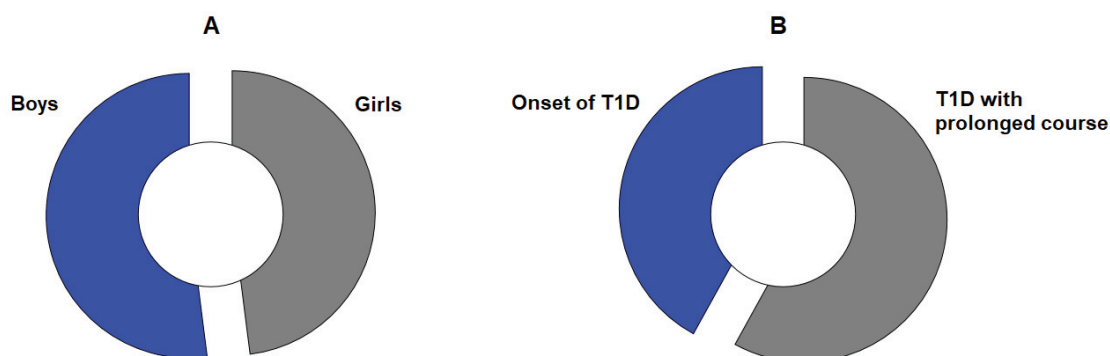


Figure 1. Gender distribution of the examined children (A); disease course distribution of the examined children (B).

The average age of those examined with type I diabetes is 12.16±1.24 years. The average age of boys was 12.07±1.21 years, the average age of girls was 13.05±0.93 years (p>0.05). Body mass index (BMI) was analyzed in

all children included in the study. The average value is 18.7±1.23 kg/m². The value of systolic blood pressure (BP) exceeded the 95th percentile for the corresponding age and group in 27.5 % of children (figure 2).

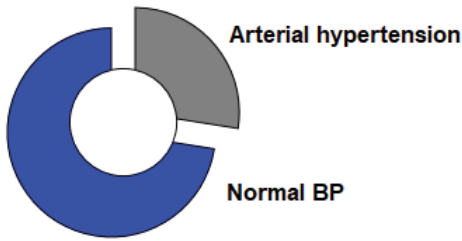


Figure 2. Distribution of examined patients based on BP.

ECG abnormalities in patients with T1D

We analyzed recordings of electrocardiograms of all examined children with T1D. So-called «small ECG abnormalities» were found. Incomplete left/right blockade bundle branch block found in 22.5 % of children, shortened PQ interval in 15 %, extrasystoles, tachycardia, bradycardia in 52.5 %, T wave amplitude decrease in 60 % (figure 3).

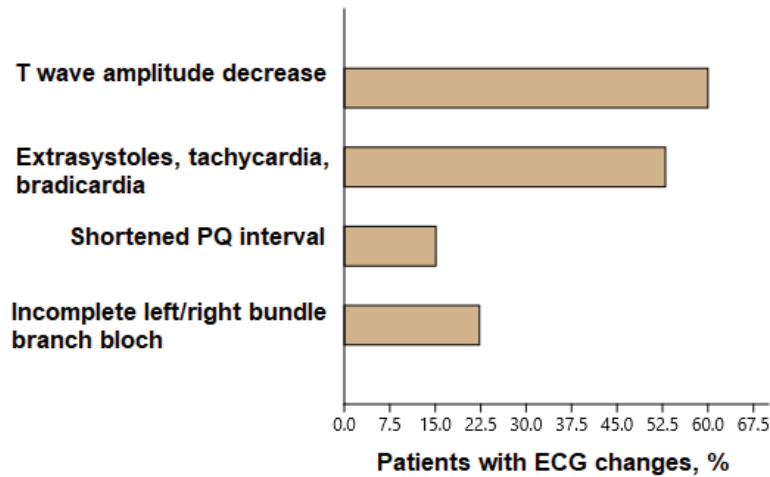


Figure 3. Main types of ECG changes in children with T1D.

Indicators of T1D compensation in examined children

We have conducted analysis of the main metabolic disorders (Hb1Ac, numbers of Ketoacidosis episodes) and peculiarities of ECG changes in relation to that. Interestingly, levels of Hb1Ac in the group with the onset of type T1D were higher as compared to patients with a prolonged disease course ($8,79 \pm 0,45$ vs. $12,3 \pm 0,41$, $p < 0,01$).

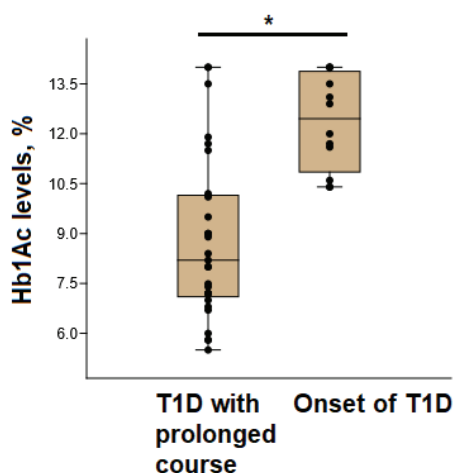


Figure 4. Hb1Ac levels in children with T1D and different disease course. Note: $p < 0,01$.

Detailed analysis shown that among all children included into the study 87.5 % of the examinees have a combination of 2-3 of the above changes on the ECG. Only 12 % of the examined children had an ECG without pathological changes. All children with newly diagnosed type 1 DM had at least 1 of the described ECG abnormalities. In contrast 84 % of children with prolonged T1D have ECG abnormalities (figure 5A). We analyzed ECG abnormalities in diabetic children and different numbers of diabetic ketoacidosis numbers/last year. All patients with 2 and more episodes of DKA/last year have at least one ECG change. In contrast 65,5 % of patients with no documented DKA during last year have ECG abnormalities (figure 5B).

Patients with diagnosed arterial hypertension do not show differences in comparison to patients without arterial hypertension in terms of frequency and quality of the ECG changes.

Correlation analysis between clinical data and ECG abnormalities in patients with T1D

We analyzed correlation between main laboratory, clinical parameters and number of ECG changes in patients with T1D using the Pearson correlation approach.

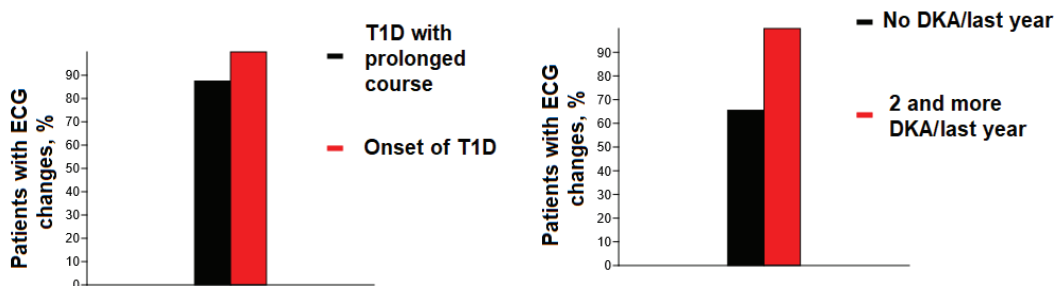


Figure 5. Frequency of ECG abnormalities in children with different disease course of T1D (A) and depending on number of DKA/last year (B).

Substantial positive correlations between Hb1Ac levels and number of ECG changes ($r = 0.85, P < 0.05$), serum cholesterol levels and number of ECG changes ($r = 0.68, P < 0.05$) were found (figure 6).

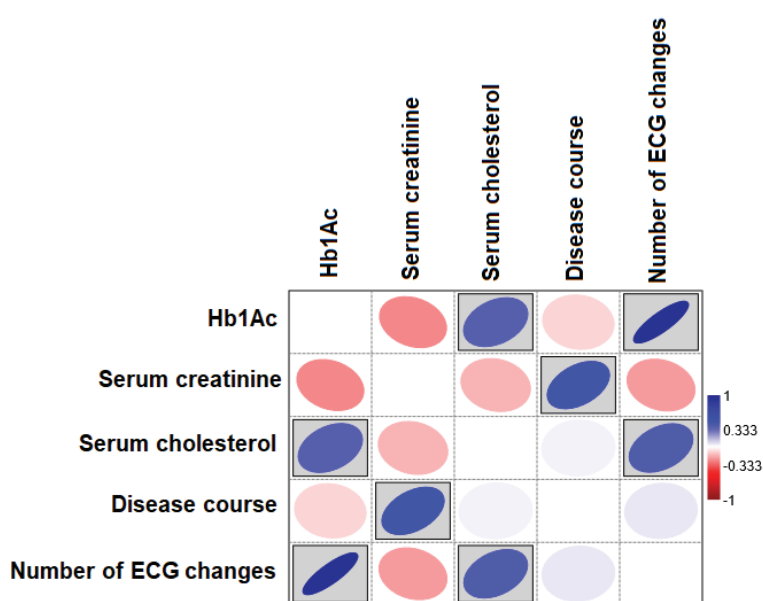


Figure 6. Correlation between main laboratory, clinical parameters and number of ECG changes in children with T1D.

DISCUSSION

It is commonly known that glycemia and cardiovascular disease are related. Even below the ranges that characterise diabetes, hyperglycemia has been linked to a higher risk of cardiovascular disease. Moreover, it has been demonstrated that hyperglycemia increases the risk of microvascular problems, some of which, like diabetic nephropathy, increase the risk of CVD [6]. Our discovery of a connection between hyperglycemia and the emergence of new abnormalities in the ECG, an objective instrument for evaluating cardiovascular health, is somewhat explained by these publications that associate hyperglycemia with CVD. It is unknown, however, whether interventions aimed at reducing glycemia will reverse ECG abnormalities [7].

In this study we show that even early in the course of diabetes mellitus (onset of T1D), ECG alterations

such as Incomplete left/right blockade bundle branch block, shortened PQ interval, extrasystoles, tachycardia, bradycardia, T wave amplitude decrease were observed in 100 % of patients.

Detailed analysis shown that among all children included into the study 87,5 % of the examinees have a combination of 2-3 of the above changes on the ECG. Only 12 % of the examined children had an ECG without pathological changes. All children with newly diagnosed type 1 DM had at least 1 of the described ECG abnormalities. In contrast 84 % of children with prolonged T1D course have ECG abnormalities.

It was previously discussed a role of diabetic neuropathy in development of CVD associated with T1D. Disrupted heart rate variability and baroreflex dysfunction are the most often occurring related disorders. Although the heart rates of patients with neuropathy were higher

and their circadian rhythms appeared to be intact, it was discovered that these patients had lower QTcs [8], moderate neuropathy with an unaltered QTc despite a reversed circadian day/night QTc rhythm.

We hypothesize that even in patients with the onset of T1D early sub-clinical signs of neuropathy have place and may have an input on ECG abnormalities development. These processes are being in parallel with basic metabolic diabetic disorders.

We analyzed ECG abnormalities in diabetic children and different numbers of diabetic ketoacidosis numbers/last year. All patients with two and more episodes of DKA/last year have at least one ECG change. In contrast 65,5 % of patients with no documented DKA during last year have ECG abnormalities. Our findings in pediatric patients are in line with other research groups.

Diabetic ketoacidosis (DKA), which is an acute complication of type 1 diabetes, is characterized by hyperglycemia, metabolic acidosis, and ketonemia. Diabetic ketoacidosis develops as a result of insulin deficiency and increased epinephrine, glucagon, cortisol, and growth hormone. The cardiovascular complications of diabetic ketoacidosis have been known for a long time. Cardiovascular complications including cardiac arrhythmia, acute myocardial infarction, and cardiac arrest may be observed during diabetic ketoacidosis and lead to sudden death syndrome [9-11]. Our correlation analysis shown positive correlations between Hb1Ac levels and number of ECG changes, serum cholesterol levels and number of ECG changes. The latter is an evidence of the potential role of metabolic changes in development of ECG changes.

CONCLUSIONS

The results of the study indicate that the majority of children with type I diabetes have so-called «small ECG abnormalities.» According to the type of disturbances, they can be classified as rhythm and conduction disturbances and combined changes. Most of the examined have a combination of 2-3 of the specified violations. Patients with onset of T1D show striking levels of ECG abnormalities in parallel with level of Hb1Ac. Study results are promising in terms of management tactics for children with type I diabetes, early detection and timely therapeutic correction of ECG abnormalities.

Study limitations and future perspectives. Our study has some deficiencies and limitations. First of all it is a limited number of patients. We conducted a cross-sectional, patient-limited pilot trial at a single site. Secondly, we did not analyze ECG changes at the time of DKA episodes which can be potentially interesting in terms of deeper understanding of the ECG changes. Study perspectives related to the development of further treatment and management approaches in children with type I diabetes in terms of early detection and timely therapeutic correction of ECG abnormalities.

FUNDING AND CONFLICT OF INTEREST

The authors report no actual or potential conflict of interest. The article was funded at the authors' own expense.

COMPLIANCE WITH ETHICAL REQUIREMENTS

The study was conducted in compliance with all relevant ethical standards including the principles of the Declaration of Helsinki. Informed consent was obtained in all cases.

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Резюме

СПЕКТР ТА ХАРАКТЕРИСТИКА ЕЛЕКТРОКАРДІОГРАФІЧНИХ ЗМІН У ДІТЕЙ З ЦУКРОВИМ ДІАБЕТОМ І ТИПУ Євгенія А. Бурлака, Інґа О. Мітюряєва-Корнійко, Марія І. Морарі, Валерія Ю. Мединська

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Вступ. Цукровий діабет І типу (ЦД1) – одне з найпоширеніших і соціально значущих захворювань. Серцево-судинні захворювання, добре відомі як супутній стан із цукровим діабетом І типу, в молодому віці проявляється рано після первинної діагностики як ознаки ремоделювання серцево-судинної системи. Зростаюча кількість даних вказує на те, що діти та молоді люди з цукровим діабетом І типу відчують субклінічну серцеву дисфункцію, мають ураження периферичних судин. Збільшення захворюваності та смертності серед дорослих пов'язують із захворюваннями периферичних артерій, серця та цереброваскулярних захворювань, а ранні судинні зміни, як було доведено, існують ще з дитинства. На сьогодні мало відомо про розвиток ранніх структурних і функціональних проблем серця у дітей із ЦД І типу. Рання діагностика має велике значення.

Мета. Оцінити частоту та спектр відхилень електрокардіографії (ЕКГ) у дітей із ЦД І типу.

Матеріали та методи. До аналізу включені історії 60 пацієнтів з цукровим діабетом І типу. Проаналізовано дані ЕКГ, основні анамнестичні, клініко-лабораторні дані.

Результати. Виявлено так звані «малі аномалії ЕКГ». Неповна ліво-права блокада ніжок пучка Гиса виявлена у 22,5 % дітей, укорочення інтервалу PQ – у 15 %, екстрасистоли, тахікардія, брадикардія – у 52,5 %, зниження амплітуди зубця Т – у 60 %. У 87,5 % обстежених на ЕКГ спостерігається поєднання 2-3 перерахованих вище змін. Лише у 12 % обстежених дітей ЕКГ була без патологічних змін. Усі діти з вперше виявленим ЦД І типу мали принаймні 1 з описаних аномалій ЕКГ. Проведено кореляційний аналіз. Були виявлені суттєві позитивні кореляції між рівнями Hb1Ac та кількістю змін ЕКГ, рівнем холестерину в сироватці крові та кількістю змін ЕКГ.

Висновки. Результати дослідження свідчать про те, що більшість дітей із діабетом І типу мають так звані «малі аномалії ЕКГ». За типом порушень їх можна класифікувати на порушення ритму і провідності та комбіновані зміни. Ці результати є перспективними з точки зору тактики ведення дітей із цукровим діабетом І типу, раннього виявлення та своєчасної терапевтичної корекції відхилень ЕКГ.

Ключові слова: цукровий діабет І типу, ЕКГ, діти, захворювання, серцево-судинна система