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Assessment of metabolic control in children with type 1 diabetes

Ocena wyrównania metabolicznego u dzieci chorujących na cukrzycę typu 1

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Abstract

Introduction: The increase in morbidity of type 1 diabetes (T1D) is observed in Poland and worldwide, particularly among the youngest patients. To prevent chronic hyperglycemia's complications, it is advised to maintain best possible metabolic control from the time of diagnosis of the disease.

Aim of the study: The purpose of this research is to evaluate adherence to medical recommendations in regard to appropriate metabolic control of T1D in children, based on Polish Diabetes Association (PTD) 2019 criteria.

Material and methods: The medical records of 388 patients with T1D hospitalized in our department between June 2018 and July 2019 were analyzed. Two hundred patients hospitalized for routine control tests were enrolled in the study. The patients were evaluated with respect to meeting the criteria for metabolic control recommended by PTD 2019 including gender, duration of disease and treatment technique. The relation between the percentage of HbA_{1c} and age, duration of the disease and lipid metabolism was studied.

Results: In the assessed group 7% of patients met all PTD's criteria of metabolic control. There was a statistically significant difference in percentage of HbA_{1c} in serum between girls and boys (12.64% vs. 26.55%, $p = 0.02$). The trend was observed between patients with T1D lasting less than or equal 3 years and those with long-standing disease (28.72% vs. 13.21%, $p = 0.007$). A significant, positive correlation was demonstrated between percentage of HbA_{1c} and low-density lipoprotein (LDL) level ($r = 0.244$), triglyceride (TG) level ($r = 0.234$) and duration of the disease ($r = 0.278$).

Conclusions: A low percentage of patients is able to achieve all aims stated by the PTD.

Key words:
children, type 1 diabetes, metabolic control.

Streszczenie

Wprowadzenie: Zarówno w Polsce, jak i na świecie obserwuje się stały wzrost zachorowalności na cukrzycę typu 1, szczególnie wśród najmłodszych pacjentów. Już od momentu rozpoznania cukrzycy u dziecka należy dążyć do osiągnięcia jak najlepszego wyrównania metabolicznego, aby zapobiec odległym powikłaniom przewlekłej hiperglikemii.

Cel pracy: Ocena wyrównania metabolicznego u dzieci chorujących na cukrzycę typu 1 zgodnie z kryteriami Polskiego Towarzystwa Diabetologicznego (PTD) z 2019 r.

Materiał i metody: Analizie poddano dokumentację medyczną 388 pacjentów z cukrzycą typu 1 hospitalizowanych w Klinice od czerwca 2018 do lipca 2019 r. Do badania zakwalifikowano 200 pacjentów skierowanych na planowe badania kontrolne. Pacjentów oceniano na podstawie kryteriów wyrównania metabolicznego według PTD z 2019 r., uwzględniając płeć, czas trwania choroby oraz sposób leczenia. Zbadano również zależność pomiędzy odsetkiem hemoglobiny glikowanej a czasem trwania cukrzycy oraz gospodarką lipidową.

Wyniki: Wszystkie kryteria wyrównania metabolicznego według zaleceń PTD z 2019 r. spełniło 7% pacjentów. Odnotowano istotne statystycznie różnice pomiędzy liczbą dziewczynek a chłopców z prawidłowym odsetkiem hemoglobiny glikowanej (12,64% *vs* 26,55%, $p = 0,02$) oraz pomiędzy dziećmi chorującymi 3 lata lub dłużej a tymi z krótszym czasem trwania cukrzycy (28,72% *vs* 13,21%, $p = 0,007$). Wykazano istotną dodatnią korelację pomiędzy odsetkiem hemoglobiny glikowanej (HbA_{1c}) a stężeniem lipoproteiny małej gęstości (LDL) ($r = 0,244$) i trójglicerydami (TG) ($r = 0,234$) oraz czasem trwania cukrzycy ($r = 0,278$).

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Wnioski: Niewielki odsetek pacjentów pediatrycznych chorych na cukrzycę typu 1 jest w stanie spełnić wszystkie kryteria wyrównania metabolicznego według PTD.
Słowa kluczowe:
dzieci, cukrzyca typu 1, wyrównanie metaboliczne.

Introduction

Type 1 diabetes (T1D) is one of the most frequent chronic childhood conditions. Nowadays, there are about 20 thousands children with T1D in Poland [1]. Epidemiological data indicate that for the past 25 years the morbidity has increased fourfold. Furthermore, children under 5 years of age are diagnosed increasingly more often.

Patients with type 1 diabetes are at risk of chronic hyperglycemia's effects from their childhood. It is related to many long – term complications such as damage and dysfunction of organs especially eyes, kidneys, nerves, heart and vessels. This is the reason why the struggle for normalization of glycemia through optimal insulin therapy is so essential [2].

Every year the Polish Diabetes Association (PTD) publishes new recommendations determining therapy strategies which enable achieving good metabolic control in terms of carbohydrate and lipid metabolism, blood pressure and body mass index (BMI). Adherence to the recommendations gives a higher chance to avoid organ complications and gives the patient a better prognosis [3].

The low percentage of patients who achieve aims stated by PTD indicates that an optimal diabetes treatment is a complex problem. Clinical experience implicates that comprehensive medical care, including multidisciplinary specialists cooperation, continual patient's re-education and active patient's participation in the therapy are essential for better metabolic control [4].

Aim of the study

The aim of the study was to evaluate adherence to medical recommendations in regard to appropriate metabolic control of type 1 diabetes in children, based on PTD 2019 criteria including gender, duration of the disease and treatment technique.

Material and methods

The medical records of 388 patients with type 1 diabetes hospitalized in our department from June 2018 to July 2019 were analyzed. Two hundred patients hospitalized for routine tests were enrolled in the study. The exclusion criteria were newly diagnosed diabetes and severe complications such as ketoacidosis or severe hypoglycemia.

The study comprises three stages. At the first stage, the whole group ($n = 200$) was evaluated with respect to meeting the criteria for metabolic control recommended by PTD 2019 (Table I) [3]. At the second stage, the analysis of achieving treatment aims stated by PTD took account of gender (girls: $n = 87$, boys: $n = 113$), duration of disease (< 3 years: $n = 94$, ≥ 3 years: $n = 106$) and treatment technique (multiple daily injections [MDI] n = 91, continuous subcutaneous insulin infusion [CSII] $n = 109$). At the last stage, the relation between the percentage of HbA_{1c} and age, duration of the disease and lipid metabolism was studied.

In the assessed group of children the girls constituted 43.5% and boys 56.5%. Distribution of age was the following: patients aged up to 7 years – 16%, 7 to 12 years – 35.5% and over 12 years – 48.5%. The average age was 11.74 ±4.2 years and average duration of diabetes was 4.46 ±3.73 years.

Statistical analysis

Shapiro-Wilk test was used to determine whether the data set is well-modeled by a normal distribution. Due to lack of normally distributed data, the U-Mann-Whitney test was used for comparing parameter's values between groups. The difference in number of children achieving aims of metabolic control in particular groups was tested by χ^2 test. The correlation between variables was calculated by Spearman test. In all tests p value < 0.05 was considered as statistically significant. All statistical analyses were conducted using the PQStat program.

Results

In the assessed group only 7% of patients met all PTD's criteria of metabolic control. The main difficulty occurred in achieving the normal percentage of glycated hemoglobin. Table II presents assessment of particular parameters.

Table I. Criteria of metabolic control according to PTD 2019

Parameter of metabolic control	Target value
HbA_{1c}	≤ 6.5%
LDL	< 100 mg/dl
HDL	> 40 mg/dl
TG	< 100 mg/dl
Blood pressure	< 90. percentile (from the age of 16 < 130/85 mm Hg)
BMI	< 85. percentile

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

The study showed that boys more often achieve good metabolic control. All PTD's criteria were fulfilled by 11 boys (9.73%) and only by 3 girls (3.45%). There was a statistically significant difference in percentage of glycosylated hemoglobin and LDL level in serum between girls and boys. Table III provides the number and percentage of girls and boys who achieved the correct value of selected parameters. Boys statistically significantly more frequently presented a correct LDL level. The average values and medians of particular parameters are shown in Table IV.

Table II. The number and the proportion of patients meeting the criteria for metabolic control recommended by PTD 2019

Parameter of metabolic control	Patients with correct parameter values	
	Study group (n = 200)	Percentage of respondents (%)
$HbA_{1c} \leq 6.5\%$	41	21%
LDL < 100 mg/dl	107	54%
HDL > 40 mg/dl	190	95%
TG < 100 mg/dl	164	82%
Blood pressure < 90. percentile	164	82%
BMI < 85. percentile	160	80%
All the criteria fulfilled	14	7%

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Patients with T1D lasting less than or equal 3 years more often met all PTD's criteria in comparison to children with long-term disease (11.70% vs. 1.87%, $p = 0.003$). The first group more frequently achieved the correct percentage of glycated hemoglobin (28.72% vs. 13.21%, $p = 0.007$). Table V provides the number and percentage of patients with varying duration of T1D who achieved correct value of particular parameters. Children with short duration of T1D have maintained the correct level of lipid profile. HDL level > 40 mg/dl were achieved by 98.94% of children and 89.62% children with long-standing disease. The average values and medians of selected parameters are presented in Table VI.

There was no statistically significant difference in metabolic control between treatment methods (MDI vs. CSII). However children treated with MDI more often met all PTD's criteria in comparison to those treated with CSII (9.89% vs. 4.59%; Tables VII and VIII). The two groups had significant difference in daily insulin requirement. It was higher among children using CSII.

Significant positive correlations were found between percentage of glycosylated hemoglobin and level of LDL ($r = 0.244$, $p = 0.0006$; Fig. 1) and TG ($r = 0.234$, $p = 0.001$; Fig. 2). Long duration of disease was correlated with worse metabolic control assessed by percentage of glycated hemoglobin ($r = 0.278$, $p = 0.00008$; Fig. 3).

Discussion

The research revealed that achieving metabolic control defined by meeting all PTD's criteria is exceptionally difficult for patients. In the assessed group only 7% of children have achieved the expected therapy results.

Table III. The proportion of patients meeting the criteria for metabolic control recommended by PTD 2019 in the gender groups

Parameter of metabolic control	Patients with correct parameter values		Statistical significance
	Girls (n = 113)	Boys (n = 87)	
$HbA_{1c} \leq 6.5\%$	11 (12.64%)	30 (26.55%)	0.02248
LDL < 100 mg/dl	38 (43.68%)	69 (61.06%)	0.01454
HDL > 40 mg/dl	85 (97.70%)	105 (92.92%)	0.12407
TG < 100 mg/dl	71 (81.61%)	93 (82.30%)	0.77111
Blood pressure < 90. percentile	78 (89.66%)	86 (76.11%)	0.01945
BMI < 85. percentile	65 (74.71%)	95 (84.07%)	0.10009
All the criteria fulfilled	3 (3.45%)	11 (9.73%)	0.0841

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Table IV. Mean values, ± standard deviations and medians metabolic control in gender groups

Parameter of metabolic control	Girls (n = 113)			Boys (n = 87)			p
	Average ±SD	Median	Min.–Max.	Average ±SD	Median	Min.–Max.	
HbA_{1c} (%)	7.57 ±1.12	7.32	6.01–11.30	7.39 ±1.37	7.13	6.02–12.70	0.11589
LDL (mg/dl)	104.04 ±26.72	103.00	58.2–223.0	94.29 ±25.34	95.90	46.0–204.0	0.00801
HDL (mg/dl)	62.84 ±14.22	61.00	28.8–104.1	62.99 ±20.35	60.90	30.8–189.9	0.52090
TG (mg/dl)	81.91 ±45.13	71.50	32.9–278.3	78.07 ±48.23	67.80	28.5–446.0	0.29894

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Table V. The proportion of patients meeting the criteria for metabolic control recommended by PTD 2019 in groups according to duration of disease

Parameter of metabolic control	Patients with correct parameter values		Statistical significance
	< 3 years (n = 94)	≥ 3 years (n = 106)	
$HbA_{1c} \leq 6.5\%$	27 (28.72%)	14 (13.21%)	0.00667
LDL < 100 mg/dl	57 (60.64%)	51 (48.11%)	0.10481
HDL > 40 mg/dl	93 (98.94 %)	95 (89.62%)	0.01616
TG < 100 mg/dl	82 (87.23%)	82 (77.36%)	0.09706
Blood pressure < 90. percentile	77 (81.91%)	91 (85.85%)	0.83751
BMI < 85. percentile	79 (84.04%)	81 (76.42%)	0.17832
All the criteria fulfilled	12 (11.70%)	2 (1.87%)	0.00261

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Table VI. Mean values, ± standard deviations and medians metabolic control in groups, in relation on the duration of the disease

Parameter of metabolic control	< 3 years (n = 94)			≥ 3 years (n = 106)			p
	Average ±SD	Median	Min.–Max.	Average ±SD	Median	Min.–Max.	
HbA_{1c} (%)	7.13 ±1.15	6.99	6.01–12.70	7.77 ±1.30	7.49	6.11–12.60	0.0001
LDL (mg/dl)	95.97 ±26.92	96.40	46.0–223.0	100.81 ±25.97	102.40	48.7–204.0	0.084
HDL (mg/dl)	64.01 ±13.43	63.25	30.8–90.7	61.96 ±21.26	58.20	28.8–189.9	0.061
TG (mg/dl)	70.75 ±26.33	65.25	28.5–170.7	87.72 ±58.71	71.20	32.2–446.0	0.073
Daily insulin requirement (j/kg m.c.)	0.63 ±0.29	0.62	0.1–1.4	0.84 ±0.27	0.80	0.2–1.8	0.0001

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Table VII. The proportion of patients meeting the criteria for metabolic control recommended by PTD 2019 in groups according to the treatment technique

Parameter of metabolic control	Patients with correct parameter values		Statistical significance
	CSII (n = 109)	MDI (n = 91)	
$HbA_{1c} \leq 6.5\%$	21 (19.27%)	20 (21.98%)	0.63615
LDL < 100 mg/dl	58 (53.21%)	49 (53.85%)	0.68787
HDL > 40 mg/dl	106 (97.25%)	84 (92.31%)	0.92854
TG < 100 mg/dl	91 (83.49%)	71 (78.02%)	0.11043
Blood pressure < 90. percentile	87 (79.82%)	77 (84.62%)	0.47189
BMI < 85. percentile	91 (83.49%)	69 (75.82%)	0.17734
All the criteria fulfilled	5 (4.59%)	9 (9.89%)	0.14328

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

Table VIII. Mean values, ± standard deviations and medians metabolic control in groups, in relation to the treatment technique

Parameter of metabolic control	CSII (n = 109)			MDI (n = 91)			p
	Average ±SD	Median	Min.–Max.	Average ±SD	Median	Min.–Max.	
HbA_{1c} (%)	7.33 ±1.000	7.25	6.01–10.69	7.64 ±1.531	7.34	6.02–12.70	0.52115
LDL (mg/dl)	98.51 ±23.81	98.40	48.7–174.6	98.56 ±29.193	97.60	46.0–223.0	0.69466
HDL (mg/dl)	63.43 ±19.66	60.40	28.8–189.9	62.33 ±15.64	61.10	30.8–99.6	0.88104
TG (mg/dl)	76.88 ±42.21	66.10	31.4–278.3	83.18 ±51.84	70.30	28.5–446.0	0.20863
Daily insulin requirement (j/kg m.c.)	0.78 ±0.20	0.77	0.3–1.4	0.70 ±0.38	0.67	0.1–1.77	0.01943

HbA_{1c} – glycated haemoglobin A_{1c}; LDL – low-density lipoproteins; HDL – high-density lipoproteins; TG – triglycerides; BMI – body mass index

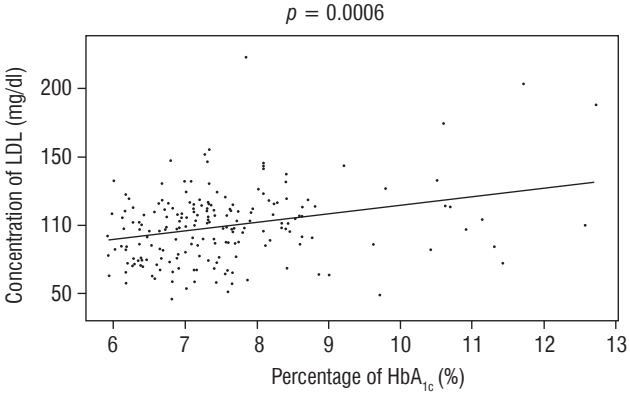

Figure 1. The correlation between the percentage of HbA_{1c} and the concentration of LDL

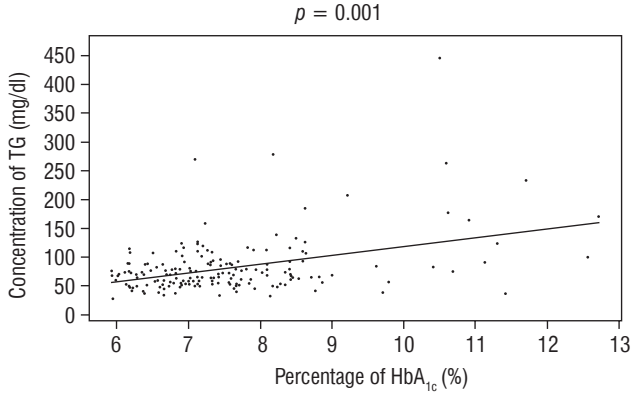

Figure 2. The correlation between the percentage of HbA_{1c} and the concentration of TG

The obtained data indicated that girls are predisposed to worse metabolic control. Similar observations involving 4000 Swedish patients below age of 18 were published by Samuelson et al. [5]. Higher BMI among girls was also confirmed by a recent and wide study on frequency of overweight and obesity among children and adolescents with type 1 diabetes. The study was performed on 3 continents by Phelan *et al.* in 2016 [6]. It is worth noting that in the Polish study of Kołodziejczyk *et al.* body mass index in girls was also higher and indicated overweight while in boys it was normal [7]. The higher BMI in girls may by caused by multiple factors such as the influence of sex hormones on parameters of carbohydrate metabolism, low level of physical activity, and concomitance of depressive disorders in comparison to boys [5–9].

The research confirmed that the duration of the disease adversely affects lipids parameters, which is consistent with other studies [9]. Long-standing diabetes predisposes to worse metabolic control assessed by percentage of glycated hemoglobin. Characteristic for diabetes lipid profile, increase of inflammatory parameters and chronic, uncontrolled hyperglycemia lead to premature atherosclerosis. These disorders justify monitoring patients to prevent macro- and microangiopathic complications [5, 10].

No clear advantage of treatment with CSII vs. MDI was found. The self-reported study showed no significant difference in percentage of glycated hemoglobin between patients treated with these methods. Moreover, applying the insulin pump does not result in lipid parameters' improvement, as was confirmed in the study carried out by Flores *et al.* [11]. According to research by Karges *et al.*, the percentage of glycated hemoglobin in children above age of 5 with T1D treated with MDI is significantly higher in comparison to those managing their diabetes by the insulin pump [12]. It is worth noting that the difference in daily insulin requirement between children treated with MDI and CSII is statistically significant. Patients treated with CSII required a higher daily insulin dose. This may be due to more frequent consumption of meals and appetizers.

Demonstrated correlation between percentage of glycated hemoglobin and level of LDL and TG indicates that hyperglycemia predisposes to secondary lipid disorders [11].

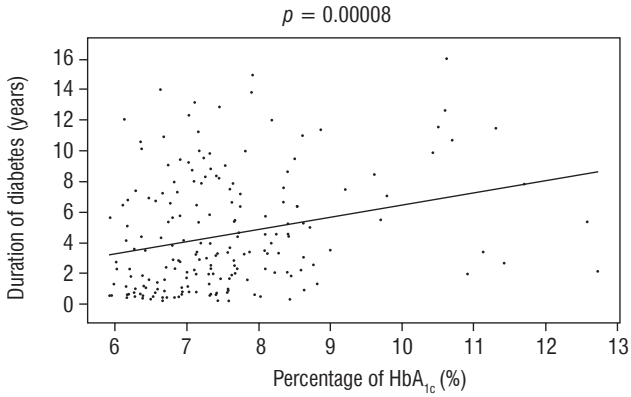

Figure 3. The correlation between the percentage of HbA_{1c} and the duration of the disease

Inappropriate metabolic control of type 1 diabetes in children may result from low awareness of the disease due to insufficient patient education. Therapeutic support with individualized and matched therapy as well as permanent re-education is crucial in striving for metabolic control [13–15].

In 2012 Pawłowska *et al.* published a study about adherence to medical recommendations in regard to appropriate metabolic control of diabetes type 1 in children hospitalized in our site, based on PTD 2006 and 2010 recommendations [16]. In their study, the average percentage of glycated hemoglobin among patients with type 1 diabetes was higher than in our current research. The increasing availability of continuous glucose monitoring systems may explain this improvement.

Conclusions

The studied group of pediatric patients with type 1 diabetes present inappropriate metabolic control. Low percentage of patients is able to achieve all aims stated by PTD. The longer duration of diabetes is associated with worse metabolic control. Continuous, regular patient's re-education and strict determination of treatment goals are indispensable.

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