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The effects of a single bout of submaximal exercise on rheological properties of the blood in children with type 1 diabetes mellitus

ABSTRACT

Background. The aim of this study was to analyze the effects of a single bout of submaximal exercise on rheological properties of the blood children with type 1 diabetes mellitus and healthy controls.

Material and methods. The study included 18 children in the age before puberty, with type 1 diabetes, both newly diagnosed (Group 1, n = 11) and with the diagnosis established at least five years earlier (Group 2, n = 7). Group 3 (n = 11) was comprised of age- and sex-matched healthy controls. Children from all the groups were subjected to progressive submaximal exercise test on a cycle ergometer. Prior to the exercise and after the test, rheological parameters of peripheral blood erythrocytes: elongation index (EI), amplitude of aggregation (AMP), half time of total aggregation ($T_{1/2}$) and aggregation index (AI) were determined.

Results. No significant differences were found between the pre- and post-exercise values of erythrocyte aggregability measures (AI, $T_{1/2}$ and AMP) and EI values at 0.30–59.07 Pa for any of the study groups.

Conclusions. These results suggest that a single bout of physical exercise exerts no unfavorable effect on erythrocyte rheology in children with type 1 diabetes mellitus. Also time elapsed since the diagnosis of type 1 diabetes mellitus does not influence rheological properties of the blood. (Clin Diabetol 2017; 6, 2: 65–69)

Key words: physical exercise, blood rheology, erythrocyte membrane, diabetes mellitus, pediatrics

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Introduction

Diabetes mellitus is a complex chronic disease which emerged as an important public health problem due to its constantly increasing incidence. According to the World Health Organization (WHO) estimates, the number of people affected with diabetes mellitus may reach 366 million in 2030, which corresponds to ca. 5% of world population [1].

The vast majority of diabetes mellitus cases belong to one of the two etiopathogenic categories: 1) type 1, associated with complete lack of insulin synthesis, resulting from destruction of Langerhans beta cells in the pancreas, and 2) type 2, linked to insulin resistance [2, 3].

The incidence of type 1 diabetes mellitus varies considerably depending on a region, from 0.61 per 100 000 annually in China to up to 41.4 per 100 000 in Finland. Alarmingly, the incidence of this type 1 diabetes mellitus in many countries has doubled during the last two decades. Type 1 diabetes represents ca. 5–15% of all diabetes cases in the United States; furthermore, it is the most common metabolic disease of the childhood, with approximately 15 000 new cases diagnosed annually [4, 5].

Diabetes mellitus is also a problem in Polish population. According to Jarosz-Chobot et al. [6], the incidence of type 1 diabetes in children has tripled during the last

15 years, and further quadruple increase is projected between 2005 and 2025, especially in the youngest age groups. A total of 1600 Polish children aged 0–14 years have been diagnosed with type 1 diabetes in 2010, and an increasing tendency in the incidence is expected, up to more than 4800 new cases in 2025 [6].

Since diabetes mellitus is generally an irreversible condition, its management is primarily aimed at attenuation of symptoms and prevention of secondary complications. Insulin therapy, appropriate diet and physical exercise regimens constituted the basis for treatment of type 1 diabetes during the last eight decades. Another vital issue is education of the patients. Physical activity as a proposal for a healthy lifestyle may exert beneficial effects on metabolic control, body weight, arterial blood pressure, self-esteem and quality of life in patients with type 1 diabetes, especially in children and young adults. Furthermore, it may reduce the risk for secondary complications, and as such should constitute a key component of lifestyle in diabetic patients [7–10]. While the effects of regular physical activity on metabolic control are well established, still little is known on the influence of high or moderate intensity short-term exercise being a common element of everyday activities in children [11].

Rheological properties of the blood are crucial for normal functioning of human body. They are determined by the number of morphotic elements (hematocrit), erythrocyte count and volume, corpuscular concentration of hemoglobin, deformability/elasticity of red blood cells determined by structural and functional properties of their membranes, and plasma concentration of protein [12].

To the best of our knowledge none of the published studies addressed comprehensively the issue of exercise-induced erythrocyte deformability in children with type 1 diabetes mellitus. Therefore, the aim of this study was to analyze the effects of a single bout of submaximal exercise on rheological properties of the blood in this group of patients.

Materials and methods

Participants

The study included 18 children with type 1 diabetes, treated and the Diabetology Outpatient Unit, Endocrinology Clinic for Children and Adolescents, Department of Pediatrics, Polish-American Institute of Pediatrics, Jagiellonian University Medical College in Krakow, both newly diagnosed (Group 1, n = 11) and with the diagnosis established at least five years earlier (Group 2, n = 7). The inclusion criteria for Groups 1 and 2 were: diagnosis of type 1 diabetes, pre-exercise blood glucose ≤ 10 mmol/L and good general status. The exclusion criteria were: cardiologic contraindications to physical exercise, presence of acetone in urine, concomitant diseases, fever. Children were before adolescence, the age of patients from both groups ranged between 9 and 11 years. The two groups did not differ significantly in terms of their body weights and sex distributions. Group 3 (n = 11) was comprised of age- and sex-matched healthy controls. Children from all the groups were subjected to progressive submaximal exercise test on a cycle ergometer.

Children from grup 1 and 2 were treated with short-acting and long-acting insulin analogues.

Methods

Prior to the testing, all qualified children and their parents were familiarized with the study protocol and written informed consent was obtained from the legal guardians. The protocol of the study was approved by the Local Ethics Committee at the Jagiellonian University Medical College in Krakow. All exercise tests were conducted under constant medical supervision.

All the participants were subjected to progressive submaximal exercise test on a cycle ergometer. The test was continued until reaching predefined heart rate (HR), corresponding to 80% of maximum heart rate (HR_{max}) calculated from the formula: HR_{max} = = 220 – age in years. To calculate individual baseline load during the test, fat-free mass (FFM) of each child was divided by 60.

Preliminary exercise test

A preliminary test was conducted two days prior to the proper exercise test on a cycling ergometer. The aim of the preliminary test was to familiarize the subjects with the testing procedure in order to minimize the level of stress and determine response to physical exercise. The test lasted ca. 2–3 min.

Proper exercise test

The proper exercise test was always conducted between 9:00 AM and 9:30 AM, after breakfast and 2.5–3 hours following injection of a short-acting insulin. The breakfast included 50–60% of energy from carbohydrates, 20–30% from fat and 20% from protein.

After the "start" command, the subject started the exercise test at a predefined pedaling rate of 60 revolutions per min (rpm). The first 3 min of the test constituted a warm-up with the load equal to 1 W × kg^{-1} FFM. Then the load was increased by 50% of the baseline value per each subsequent 3-min increment. The test was terminated after the patient reached HR corresponding to 80% of his/her HR_{max}. HR was monitored continuously and recorded every 0.5 min.

Measurements

Exercise tests were conducted on Monark 818E cycle ergometer (Sweden). HR was determined with Vantage NT monitor (Polar-Electro, Finland). Body height (BH) was measured with a Martin type anthropometer. Body mass (BM), percentage of body fat (%F), fat mass (FM) and fat-free mass (FFM) were determined with Tanita Body Composition Analyzer, model TBF-300.

Rheological parameters

The analysis included peripheral blood erythrocytes from patients and controls. Prior to the exercise and after the test, blood samples, 5 ml each, were collected from an antecubital vein to $EDTAK_2$-coated tubes, placed at +4°C and transferred to the Laboratory of Pathology of Musculoskeletal System, University School of Physical Education in Krakow.

Rheological parameters of erythrocytes: elongation index (EI), amplitude of aggregation (AMP), half time of total aggregation ($T_{1/2}$) and aggregation index (AI) were determined with Laser-Assisted Optical Rotational Cell Analyzer (LORCA)-type rheometer.

Statistics

The results were subjected to two-way repeated measures ANOVA. The effects of independent variables were considered significant at $p < 0.05$. Statistical characteristics of the analyzed variables for each of the study groups were presented as arithmetic means and their standard deviations (SD).

Results

Statistical characteristics of the analyzed rheological parameters, EI at 0.30–59.97 Pa shear stress, AI, $T_{1/2}$ and AMP, for each of the study groups are presented in Tables 1–2.

No significant differences were found between the pre- and post-exercise values of erythrocyte aggregability measures, AI, $T_{1/2}$ and AMP (Table 1). Similarly, no significant exercise-induced changes were observed in EI values at 0.30–59.07 Pa for any of the study groups (Table 2).

Discussion

According to DeMarco et al. [13], a pre-exercise meal with low glycemic index may positively affect maximal performance after a sustained exercise. Moreover, these authors showed that meals with low glycemic index maintain higher plasma glucose levels during the exercise than those with high glycemic index [13]. Our patients were always subjected to the proper exercise test after breakfast, between 9:00 AM and 9:30 AM, 2.5–3 hours following the injection of a short-acting insulin.

High intensity physical exercise induces a number of changes in the rheological properties of the blood, namely an increase in plasma viscosity, hematocrit level and AI values, as well as a decrease in EI and $T_{1/2}$. A post-exercise meal was shown to cause further decrease in EI values, which corresponded to greater rigidity of erythrocytes, but without concomitant changes in their aggregability and viscosity of the plasma [14, 15]. According to Monnier et al. [16], also hydration and dehydration may significantly affect rheological properties of the blood, specifically erythrocyte elongation and aggregability.

We did not observe significant changes in erythrocyte deformability in our children with type 1 diabetes and healthy controls. Consequently, a single bout of submaximal exercise does not necessarily induces unfavorable changes in EI, and thus does not promote an increase in the erythrocyte membrane rigidity. Diabetes mellitus may lead to many alterations of both erythrocyte membranes and cytosol. Each of these changes may result in the loss of erythrocyte deformability. The latter can be also decreased due to progression of the primary disease and cellular aging [17]. Erythrocytes from patients with diabetes mellitus were shown to be more rigid than those from healthy persons, and rheological alterations, namely greater aggregability and

Table 1. Mean (± SD) values for amplitude of erythrocyte aggregation (AMP), half time of total aggregation ($T_{1/2}$) and aggregation index (AI) determined prior to and after the exercise test in patients with type 1 diabetes mellitus (group 1, newly diagnosed, and group 2, diagnosed at least 5 years earlier) and healthy controls (group 3)

Parameter	Test	Group 1	Group 2	Group 3	p
AMP	Pre	22.040 ± 0.930	20.641 ± 1.260	20.808 ± 0.930	0.279
	Post	21.667 ± 0.958	23.010 ± 1.298	21.132 ± 0.959	0.327
$T_{1/2}$	Pre	3.693 ± 0.609	3.065 ± 0.824	3.751 ± 0.609	0.667
	Post	3.535 ± 0.681	3.225 ± 0.922	3.993 ± 0.681	0.603
AI	Pre	53.003 ± 3.148	55.173 ± 4.262	53.797 ± 3.148	0.642
	Post	51.925 ± 3.072	56.896 ± 4.159	54.725 ± 3.072	0.566

Table 2. Mean (± SD) values for erythrocyte elongation index determined prior to and after the exercise test in patients with type 1 diabetes mellitus (group 1, newly diagnosed, and group 2, diagnosed at least 5 years earlier) and healthy controls (group 3)

Shear stress (Pa)	Test	Group 1	Group 2	Group 3	p
0.30	Pre	0.037 ± 0.010	0.041 ± 0.013	0.071 ± 0.010	0.340
	Post	0.033 ± 0.010	0.033 ± 0.013	0.075 ± 0.010	0.240
0.58	Pre	0.050 ± 0.010	0.057 ± 0.013	0.096 ± 0.010	0.572
	Post	0.045 ± 0.010	0.056 ± 0.012	0.108 ± 0.010	0.095
1.13	Pre	0.097 ± 0.010	0.091 ± 0.013	0.094 ± 0.010	0.912
	Post	0.092 ± 0.010	0.089 ± 0.013	0.098 ± 0.010	0.604
2.19	Pre	0.190 ± 0.019	0.175 ± 0.023	0.163 ± 0.018	0.963
	Post	0.187 ± 0.019	0.175 ± 0.023	0.166 ± 0.018	0.803
4.24	Pre	0.304 ± 0.021	0.283 ± 0.027	0.263 ± 0.021	0.882
	Post	0.300 ± 0.021	0.285 ± 0.026	0.266 ± 0.021	0.817
8.23	Pre	0.411 ± 0.020	0.387 ± 0.026	0.362 ± 0.020	0.757
	Post	0.409 ± 0.020	0.391 ± 0.025	0.364 ± 0.020	0.737
15.96	Pre	0.493 ± 0.018	0.470 ± 0.022	0.443 ± 0.017	0.767
	Post	0.490 ± 0.017	0.474 ± 0.022	0.444 ± 0.017	0.556
31.04	Pre	0.551 ± 0.015	0.531 ± 0.018	0.508 ± 0.014	0.558
	Post	0.548 ± 0.014	0.536 ± 0.018	0.509 ± 0.014	0.226
59.07	Pre	0.588 ± 0.012	0.572 ± 0.014	0.556 ± 0.011	0.603
	Post	0.585 ± 0.011	0.577 ± 0.014	0.558 ± 0.011	0.346

lower deformability predispose individuals with type 1 diabetes mellitus to microcirculatory disorders [1].

Our participants did not show significant differences in their pre- and post-exercise values of erythrocyte aggregability indices (AI, AMP, $T_{1/2}$). This implies that a single bout of submaximal exercise neither enhanced the aggregability of erythrocytes nor influenced the rate of their aggregation in the three studied groups, which should be considered a positive finding. Koszela and Szyguła [18] documented beneficial effects of controlled physical exercise on compensation of type 1 diabetes mellitus. Also Tansey et al. [19] confirmed that physical exercise may exert beneficial effects in subjects with this condition. They observed that adolescents with type 1 diabetes presented with lower plasma concentrations of glucose when subjected to a sustained moderately-intense physical exercise; furthermore, the training significantly reduced the risk for hypoglycemia in the subjects with baseline concentrations of glucose < 120 mg/dL. Finally, the authors of this study concluded that treatment with 15 g of oral glucose may be often insufficient to control exercise-induced hypoglycemia in adolescent patients. In contrast, Admon et al. [7] did not observe any beneficial effects of physical exercise in patients with type 1 diabetes mellitus who exercised with insulin pumps or without. Furthermore, their patients, especially those using insulin pumps, more often presented with late hypoglycemia than hypoglycemia during exercise. Therefore the authors recommended to turn off the pump during prolonged exercise, and to monitor blood concentration of glucose for several hours post-exercise, regardless of the pump type [7].

Our study documented the spectrum of exercise-induced changes taking place in erythrocytes from patients with type 1 diabetes, as well as their relationship with duration of the disease. However, none of the hereby observed associations were statistically significant, which justifies further research on a larger group of subjects to understand in detail the effects of physical exercise on rheological properties of the blood in patients with type 1 diabetes mellitus.

Conclusions

1. Children with type 1 diabetes mellitus, either newly diagnosed or established one, did not show statistically significant differences in their pre- and post-exercise indices of erythrocyte elongation and aggregability.
2. Time elapsed since the diagnosis of type 1 diabetes mellitus does not influence rheological properties of the blood.
3. Lack of significant changes in erythrocytes from children with newly diagnosed and established type 1 diabetes implies that a single bout of physical exercise exerts no unfavorable effect of rheology of these cells.

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