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Original Research Article

Lipid peroxidation and antioxidant protection in girls with type 1 diabetes mellitus during reproductive system development

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ABSTRACT

Background and objective: Type 1 diabetes mellitus (T1D) is found worldwide and is regarded as one of the main risks to human health. The objective of this study was to determine the state of lipid peroxidation (LPO) and antioxidant protection in girls with T1D type considering the stages of reproductive system development.

Materials and methods: This study enrolled 56 young girls with T1D and 60 healthy girls (control) matched by age. The study population was divided into 3 age groups: prepubertal, adolescent, and juvenile. The state of LPO and antioxidant system was assessed using the coefficient of oxidative stress that represented the ratio of LPO products to general antioxidative blood activity. Spectrophotometric and fluorometric methods were applied.

Results: The results of our study showed increased conjugated diene (CD) and thiobarbituric acid reactant (TBAR) concentrations as well as a decreased reduced glutathione level in prepubertal girls with T1D. Adolescent girls with T1D had a significantly greater CD level and juvenile girls with T1D had a significantly greater TBAR level and lower α-tocopherol concentration than girls in the control group. The greatest coefficient of oxidative stress (1.16) was observed in the prepubertal period.

Conclusions: The prepubertal period is characterized by the most severe state of lipid peroxidation process–antioxidant protection.

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1. Introduction

Type 1 diabetes mellitus (T1D) is found worldwide and is regarded as one of the main risks to human health [1]. T1D is characterized by varying levels of morbidity in different populations and its prevalence increase in the majority of developed countries during the last 30 years [2,3]. The manifestation and development of T1D in girls often occurs during formation of reproductive system (in Russia from 20% to 50% of patients under 15 years of age) [4]. This pathology may affect the tempo and course of pubertal growth and development, onset of menarche and the violation of menstrual function in girls [5]. Pubertal changes induce glucose metabolism or specific insulin resistance. Recent data has shown that puberty greatly increases the risk of diabetes complications and the management of this transitional age is critically important [6]. It is well known that oxidative stress (OS) is known as a component of molecular and cellular tissue that damage mechanisms in different human diseases [7,8]. The results of many clinical and experimental studies have suggested that lipid peroxidation processes are activated during different stages in different types of T1D, even in their subclinical forms [9]. The existence of hyperglycemia produces increases OS via nonenzymatic glycation, glucose autoxidation and alterations in polyol pathway activity with subsequent influence at the whole organism [10]. Many authors have observed increase OS at the early and late stages of T1D in girls [11]. It is known that certain indices of OS due to the duration of diabetes and the efficacy of glycemic control [12]. Some studies have showed that puberty in girls modulates antioxidant mechanisms of childhood diabetes that may have implications for the treatment and interventions [13]. The aim of the present study was to evaluate the state of lipid peroxidation (LPO) and antioxidant defense (AOD) in patients – girls with T1D considering stages of reproductive system development.

2. Materials and methods

2.1. Study subjects

Parameters of LPO and AOD system were measured in blood samples of 56 young girls with T1D with no clinical diabetic angiopathy and 60 healthy girls (control) matched by age. All of the patients lived in Irkutsk city (East-Siberia). The study population was divided into 3 age groups: prepubertal (7–13 years), adolescent (14–15 years), and juvenile (16–18 years) girls. The criteria for compensation of T1D at young girls were used recommendations International Society for Pediatric and Adolescent Diabetes (ISPAD) Consensus Guidelines, 2000. All groups of patients with T1D were matched for diabetes duration, glycemic control, cholesterol and triacylglycerole levels. There were no significant differences in age and number between the control group and patients with T1D. The baseline characteristics are presented in Table 1. There were no significant differences in diet habits and physical activity between the patients of all groups. All patients with T1D got insulin replacement therapy. Patients with severe somatic pathology and severe diabetic complications (chronic renal failure, macroangiopathy) were excluded out of this study. This study was approved by the Ethic Committee of Scientific Centre of family health and human reproduction problems (Siberian Branch of Russian Academy of Medical Sciences), and all participants provided patients signed written informed consent.

2.2. Study methods

Patients' blood samples were collected after 12-h overnight fasting, centrifuged for 5 min at $1.500 \times g$ at 4 °C, and erythrocytes were washed three times with NaCI 0.9% (wt/vol). Aliquots of ethylenediaminetetraacetic acid plasma and washed erythrocytes were used immediately or kept frozen in −40 °C, but not more than one month. Lipid peroxidation, estimated in terms of the concentration of conjugated dienes (CDs) and thiobarbituric acid-reactive substances (TBARS) in plasma of blood. The CDs concentrations were detected on absorbance of plasma heptanes extracts at 232 nm [14]. We used the coefficient of molar absorption ($K = 2.2 \times 10^5\ M^{-1}\ C^{-1}$) for conversion of absorption units to μmol/L. Thiobarbituric acid reactants (TBARs) levels were detected by fluorometry [15]. The supernatant, prepared as given for determination of enzymes, was mixed with 29 mM 2-thiobarbituric acid (TBA) in 8.75 M acetic acid and heated at 95 °C for 1 h. After cooling, TBARS were extracted to n-butanol and the fluorescence of the organic layer was measured at 515 nm (excitation) and 554 nm (emission). The concentration of TBARS was estimated by referring to the standard 1,1,3,3-tetraetoxypropane and

Table 1 – Baseline characteristics of diabetic and control subjects.

Clinical data	Stages					
	Prepubertal		Adolescent		Juvenile	
	T1D ($n = 13$)	Control group ($n = 13$)	T1D ($n = 30$)	Control group ($n = 24$)	T1D ($n = 17$)	Control group ($n = 19$)
Age, years	10.69 ± 2.10	11.08 ± 1.85	14.90 ± 0.80	14.63 ± 0.77	17.59 ± 1.50	17.16 ± 1.21
Duration of disease, years	3.15 ± 2.4	–	3.54 ± 1.45	–	3.21 ± 1.65	–
Hb A_{1C}, %	9.77 ± 2.32	–	9.58 ± 2.22	–	9.74 ± 2.61	–
Cholesterol (mmol/L)	4.75 ± 1.30	4.30 ± 1.32	4.44 ± 1.19	4.25 ± 1.24	4.80 ± 1.12	4.35 ± 0.91
Triacylglycerols (mmol/L)	0.82 ± 0.36	0.64 ± 0.22	0.72 ± 0.48	0.56 ± 0.21	0.74 ± 0.33	–

Values are means ± standard deviation.