

Non-Enzymatic Glycation in the Assessment of Metabolic Compensation of Diabetes Mellitus in Children

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ABSTRACT

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Background

Type 1 diabetes mellitus (DM) is one of the most common chronic metabolic diseases. According to the International Diabetes Federation, the average annual increase in morbidity in most European countries is about 3.4%. Considerable attention is currently being paid to the study of specific vascular pathology in DM, pathogenetic mechanisms, the nature of cellular damage, early markers of occurrence and progression.

Aims

To establish the diagnostic significance of the concentration of soluble receptors of protein glycation end products (sRAGE) in children with type 1 diabetes mellitus. Materials and methods: conducted a cross-sectional comparative descriptive study, determined by ELISA and analyzed the performance of plasma

soluble receptor of advanced glycation end products of proteins (sRAGE) in patients with type 1 diabetes of both sexes from 6 to 17 years with disease duration of 1-10 years, studied correlation of sRAGE and levels of glycated hemoglobin with the use of multivariate regression analysis in the group of patients with diabetes.

Results

The content of sRAGE in the blood was determined in 69 patients, of which 38 patients with type 1 diabetes (group 1), 31 were children of the first and second health groups without carbohydrate metabolism disorders (group 2). In patients with diabetes, it was mandatory to study the level of glycated hemoglobin (HbA1c). The indicators of plasma soluble receptors of protein glycation end products (sRAGE) in the study groups were analyzed [1]. Since the

concentration of sRAGE in group 1 patients did not have a normal distribution on a uniform scale, this parameter was considered on the logarithmic $\ln(\text{sRAGE}(\text{pg/ml}))$ scale (Table 1). The results of the study revealed a significant decrease in the concentration of sRAGE in the plasma of patients with diabetes mellitus ($p < 0.05$) [2]. Thus, the average, maximum and minimum sRAGE levels in group 1 were 1460, 2826 and 592 pg/ml against similar indicators in group 2 -

1741, 2924 and 1056 pg/ml, respectively (Table 1). The median sRAGE values in group 1 patients corresponded to 1391 pg/ml, in children 2 groups - 1636 pg/ml. Analysis of the content of glycated hemoglobin in the serum of patients with DM showed unsatisfactory compensation of carbohydrate metabolism [3]. The average level of HbA1c in the study group was 9.36% with a minimum value of 5.9%, a maximum of 14.1% (median - 9.32).

Table 1: sRAGE values in the normal and logarithmic scale and the Shapiro-Wilk normality criterion in the examined patients.

	Mean	Median	Minimum	Maximum	Std.Dev.	Shapiro-Wilk W	Shapiro-Wilk p
1 group (n=38)							
sRAGE(pg/ml)	1460	1391	592	2826	557	0,915	0,016
Ln (sRAGE (pg/ml))	7,219	7,238	6,384	7,947	0,374	0,972	0,575
HbA1C (%)	9,36	9,32	5,9	14,1	1,96	0,974	0,644
2 group (n=31)							
sRAGE(pg/ml)	1741	1636	1056	2924	490	0,94	0,217
Ln (sRAGE (pg/ml))	7,426	7,4	6,963	7,981	0,2736	0,98	0,887

It is likely that the decrease in the concentration of sRAGE in patients with DM is due to an increase in RAGE due to hyperglycemia, as well as a violation of the cleavage of sRAGE from RAGE, which may be mediated by endogenous insulin deficiency and secondary insulin resistance [4]. The data obtained suggest that low sRAGE values in patients with DM mark the degree of activation of the RAGE system and reflect the individual risk of vascular pathology [5]. The correlation between the level of sRAGE and glycated hemoglobin was studied using multivariate regression analysis in a group of patients with diabetes mellitus [6]. The results of the study revealed the dependence of the sRAGE indicator on the combined influence of several factors [7]. A significant regression model was found predicting the concentration of sRAGE by the level of glycated hemoglobin and puberty [8]. There were no gender differences with the changed sRAGE values [9]. The presented data reflect the peculiarities of the influence of puberty on the metabolic compensation of diabetes [10-15]. It is known that the period of puberty is normally characterized by physiological insulin resistance and an increase in the secretion of counterinsular hormones. These circumstances make it difficult to achieve the target values of glycemia in adolescents with diabetes [16-18].

The obtained data of the performed analysis established a significant effect on the concentration of sRAGE of a combination of elevated HbA1c and adolescence and allow us to attribute the puberty period to special risk factors in the formation of negative "metabolic memory" and in the occurrence of diabetic microangiopathies [19-21]. To study the relationship between sRAGE and HbA1c indicators in children with diabetes mellitus, an inverse regression model was created [22]. The results showed an inverse correlation and allowed the calculated level of HbA1c to

be indicated by the concentration of sRAGE, gender and age [22]. The presented data reflect the diagnostic significance of soluble receptors of protein glycation end products in the assessment of metabolic memory and allow us to consider sRAGE as a predictor of the formation of glucose toxicity in children with type 1 diabetes mellitus [23].

Discussion

In this paper, the indicators of plasma soluble receptors of protein glycation end products (sRAGE) in children with diabetes mellitus are analyzed. A significant decrease in the plasma concentration of sRAGE was found in patients with the pathology under consideration ($p < 0.05$), which is probably due to an increase in the expression of receptors for protein glycation end products (RAGE) due to hyperglycemia, as well as a violation of the cleavage of sRAGE from RAGE, mediated by endogenous insulin deficiency and secondary insulin resistance. In a group of patients with diabetes mellitus, the correlation between the level of sRAGE and glycated hemoglobin was studied using multivariate regression analysis. The dependence of the sRAGE indicator on the combined influence of several factors is revealed [22]. The combination of elevated HbA1c and adolescence has been found to have the most significant effect on the sRAGE concentration, which makes it possible to attribute puberty to modifiable risk factors in the formation of negative metabolic memory and in the occurrence of diabetic microangiopathies [24].

To study the relationship between sRAGE and HbA1c indicators in children with diabetes mellitus, an inverse regression correlation model was created that allows determining the calculated level of HbA1c by sRAGE concentration, gender, and age [24]. The presented

data reflect the diagnostic significance of soluble receptors of protein glycation end products in the assessment of metabolic memory. Thus, the performed study made it possible to assess the level of plasma sRAGE in type 1 diabetes mellitus, to present an analysis of the functional relationship between the values of HbA1c, sRAGE, gender and age-sex factors, to clarify the diagnostic significance of sRAGE for determining metabolic compensation and early detection of the risk of vascular pathology in childhood [25]. The authors declare the absence of obvious and potential conflicts of interest related to the publication of this article.

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