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CLINICAL AND LABORATORY CHANGES IN DIABETIC NEUROPATHY IN ADOLESCENTS

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Annotation
Today, 100,000 children and adolescents suffer from diabetes mellitus (DM) in the world. Pediatric diabetic (DN) neuropathy is considered the least studied area. With late diagnosis of the disease, progression of DN occurs, manifested by a lack of alertness in relation to peripheral neurological complications, leading to the development of disability. Relevant is the search for genetic markers, neuroimmunological parameters, links with clinical and neurophysiological parameters in children with DM, which helps to identify a group of children and adolescents at risk of developing DN, as well as prevention and treatment in the early stages of complications of this disease.

Keywords: diabetes mellitus, diabetic neuropathy, children, cerebral neurological factors, ciliary neurological factors.

Introduction

Today, more than 100,000 children and adolescents in the world suffer from diabetes. The peak incidence occurs in early puberty. Moreover, the pathogenetic bases of specific complications are quite high, up to 90% (3, 8). Diabetic neuropathy (DN) is the most common, and at the same time, little studied complication of diabetes in childhood. The low visibility of DN in childhood is associated with diagnostic difficulties due to non-severe, including subclinical (asymptomatic) course options; the diagnostic process itself is limited, since the main diagnostic methods for detecting DN have been created for the adult population. The progression of DN, with late diagnosis of the disease, lack of alertness in relation to peripheral neurological complications, leads to the development of disability (2, 7). These facts make it necessary to develop methods for diagnosing DN, taking into account age

characteristics, type of DM, severity and prognosis. Effective methods of therapy and rehabilitation of children with DN require new pathogenetic substantiated approaches (1, 6). In the adult population, complications depend on duration, on insulin resistance, in childhood, as shown in the literature, do not depend on glycemic control, duration or type of diabetes mellitus. Accordingly, the search for genetic markers, neuroimmunological parameters, and the relationship with clinical and neurophysiological parameters in children with DM is relevant, and can help identify a group of children and adolescents at risk of developing DN, prevention and therapy in the early stages of complications (5, 8, 4) . Objective. To study the state of cerebral and ciliary neurological factors in children and adolescents with diabetic neuropathy. Material and research methods. The study included children and adolescents from 8 to 18 years of age with diabetes mellitus, regardless of type. The control group included children and adolescents of the same age without diabetes mellitus - 15. In addition, the study included children and adolescents with inflammatory polyradiculoneuritis - 20. Children and adolescents with diabetes mellitus out of 100 children were included in the study only patients with sensorimotor polyneuropathy - 42, among of them, patients with a subclinical form - 19, a clinical form - 23 were identified. The examination was carried out for the period 2020-2022, on the basis of the endocrinological hospital of Samarkand and on the basis of the 1st clinic of the SamMU Department of Pediatric Neurology. All children underwent a standard clinical and neurological examination, an instrumental method for the study of ENMG, the functional scales TSS (general scale of neurological symptoms, modified according to the age of patients, if necessary) and the NDS scale (neuropathic dysfunctional score) were studied. Laboratory analysis, taking into account the goal, assumed the determination of ciliary and brain-derived neurotrophic factor. Statistical data were processed on an individual computer using standard Student's criteria.

Research results. Researchers of many scientific studies have found that neurotrophic factor plays an important role in protecting and supporting the peripheral nervous system, it also helps to strengthen myelin with Schwann cells. And since Schwann cells have a powerful effect on axons, there is a suspicion that it is the deficiency of the level of neurotrophic factor that contributes to the deterioration and progression of peripheral nerve damage against the background of diabetes mellitus. In the described groups, neurotrophic factors such as ciliary (CF) and cerebral (BF) were studied. According to the results, CF (ciliary) factor in DIP, on average, showed 21.0 pg/ml, in healthy children this figure was 10.9 pg/ml, but in children with PVH it corresponded to 19.5 pg/ml, where p = 0.001. At the same time, the brain-derived

neurotrophic factor (BF) in DIP with SMP is on average 9578 pg/ml, in healthy children the results are close to the norm of 6233 μg/ml, and the most interesting thing is that in children with PVG they were changed and corresponded to 9379 pg/ml , which is p=0.0001 in significance. When analyzing neurotrophic factors in D and P, depending on the type of DM, it turned out that in children with D&P with type 2 DM, the factor was significantly higher. Thus, in DIP with SMP with type 1 diabetes, BF is on average 9052 pg/ml, and in type 2, on average, 9574 pg/ml, where p = 0.001. At the same time, in the subclinical stage, on average, the BF figures were within 8778 pg/ml, and in the clinical stage 9400 pg/ml, where p=0.0001.

As for changes in the brain neurotrophic factor depending on the duration of the disease, for more than 10 years there has been a slight decline to a decrease and is equal to 9393 pg/ml, most likely this fact is associated with adaptation to the disease over a fairly long period. But what cannot be said about the ciliary neurotrophic factor, where CF reacts to a long period of the disease with an increase in indicators, by 10%, which had an average limit of 30.9 pg/ml, p=0.0001.

Again, the statistical correlation required to control the relationship between neurotrophic factor, clinic and instrumental data revealed a close relationship between the studied parameters, where CF and BF, R=0.76, p=0.002. This means that the results obtained confirm the connection and direction in the same mode, which unites them as the pathogenetic nature of the disorder. As in previous studies, interest in changing depending on the duration of the disease, the level of glycated hemoglobin, and the form of the disease. In patients where the duration of the disease did not exceed 10 years, a rise in the level of brain-derived neurotrophic factor up to 9680 pg / ml was naturally observed, and when the duration of the disease exceeded the limit of 10 years (12-15 years), a characteristic decrease in BF values to 9250 was noted. the level of ciliary neurotrophic was statistically consistently high in patients with 5 years and more than 10 years of diabetes mellitus. Depending on the form of the disease, the following indicators were found, in the subclinical form, the detected concentrations of BF were within 9570 and CF 25.8 pg / ml, that is, an increase in numbers on the face, which suggests the likelihood of an early reaction of the Schwann cell factor in response to the initial stage of axonopathy, for the regeneration of peripheral nerve disorders. Of course, the brain-derived neurotrophic factor also reacts to the level of high (compared to the control indicator) glycated hemoglobin, the higher the blood sugar, the higher the BF; But the ciliary neurotrophic factor is increased even with a relatively stable (slightly high) level of glycated hemoglobin, HbA1 and CF, R=-0.26, p=0.04. An interesting fact was that in patients where the electroneuromyography parameters were not changed, a change in CF was noted,

which made it possible to evaluate these patients as having a subclinical form of the disease, respectively, the CF indicator can be considered a test for predicting and determining the complications of diabetes in children and adolescents, at an early stage.

In patients examined with a clinical form, older than 15 years, with a long duration of the disease, a high BF=9895 pg/ml and a low CF=19.9 pg/ml were characteristic. The correlation between this category of patients with instrumental changes on ENMG revealed a very low M-response rate, <0.55 mV, and on CRV, <39 m/s, which gives half the difference between the norm. This means that there is a progression and a deminilizing process.

Table 1 Analysis of neurotrophic factor in the examined groups (pcg/ml)

Indicators SR	SPM		PVG	Healthy	P
	Subclinical	Clinical			
Bf	21,0		19,5	10,9	0,001
Average BF	9578		9379	6233	0,0001
Indicators	8778	9400			0,0001

Correlation analysis with the indices of electroneuromyography at the subclinical stage indicates elevated BF indices and no change in ENMG indices, that is, the level of brain-derived neurotrophic factor can serve as an early marker for diabetic sensorimotor polyneuropathy. The level of ciliary neurotrophic factor in comparison with ENMG indicators in the subclinical stage were identical, CF increased, without changes in myographic parameters, which is also the basis for conducting these analyzes in DIP with DM for the diagnosis of early forms of sensorimotor polyneuropathy. And the interconnected concentration of ciliary and brain-derived neurotrophic factor within the correlation direct indicator, where p=0.0002, indicates a presumed violation of the peripheral nervous system.

Without stopping there, a curve of changes in ciliary neurotrophic was compiled, in order to determine the development of the severity into the clinical stage, as an indicator of prognosis. It turned out that the lower the CF, the worse the indicator of clinical signs of diabetic polyneuropathy, in such cases, the ciliary neurotrophic factor should not exceed 6 pg/ml. in correlation analysis with ENMG, which is considered indicative in the clinical stage. The study of ciliary neurotrophic factor at the moment needs a little to confirm the diagnosis, but a lot to identify a long-term prognosis and, accordingly, determine the tactics of treatment. In order to get an even more complete

model of the interaction of neurotrophic factors with the results of other indicators depending on the form of the disease, the decision was to make a connection with testing by scales. The results of the correlation analysis on the TSS scale (general scale of neurological symptoms), where the indicators were in the range from 3.5 to 7.5 points (average 5.5), with indicators of the neurotrophic factor, in the subclinical form of SMP, the relationship according to the degree of prognosis, that is, in the absence of the ability to use laboratory tests, with the same success, indicators on scales can serve as an effective prognosis in making a diagnosis. But only in the aggregate study of indicators of several scales, for example, the use of the NDS scale (neuropathic dysfunctional score), which showed the reliability of sensorimotor disorders from the severity of the disease and was in the range from 10 to 14 points. The severity of diabetic polyneuropathy on the NDS scale had statistically significant correlations with neurotrophic factors, which can also be used as one of the evidence in this category of patients. The only weak link in assessing the reliability of the results obtained is the age of children, where the patient cannot always correctly and clearly assess the level of damage, respectively, questionnaires on scales, and an electroneuromyographic examination cannot be final in making a diagnosis, its form and severity, thus the laboratory nature of recognition is the most indicative.
FINDINGS

1. Correlation analysis with the indices of electroneuromyography at the subclinical stage indicates elevated BF indices and no change in ENMG indices, that is, the level of brain-derived neurotrophic factor can serve as an early marker for diabetic sensorimotor polyneuropathy.
2. The severity of diabetic polyneuropathy on the NDS scale had statistically significant correlations with neurotrophic factors, which can also be used as one of the evidence in this category of patients.

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