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Aspects of Diabetic Neuropathy in Adolescence

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Abstract: Today, more than 100,000 children and adolescents worldwide have DM. The peak of morbidity falls on the early pubertal period. Moreover, the pathogenetic basis of specific complications is quite high, up to 90% (3, 8). Diabetic neuropathy (DN) is the most frequent and at the same time poorly studied complication of DM in childhood. The low visibility of DN in childhood is due to the difficulties in diagnosis, due to the non-severe, including subclinical (asymptomatic) variants of the course; the diagnostic process itself is limited, as the main diagnostic methods for detecting DN have been developed for the adult population.

Keywords: diabetic neuropathy, adolescence, diabetes mellitus, disability.

Introduction. Progression of DN, in case of late diagnosis of the disease, lack of vigilance towards peripheral neurological complications, leads to the development of disability (2, 7). These facts make it necessary to develop methods of diagnostics of DN taking into account age features, type of DM, severity and prognosis. Effective methods of therapy and rehabilitation of children with DN require new pathogenetic approaches (1, 6). In adults, complications depend on duration, on insulin resistance, in children, as the literature shows, do not depend on glycaemic control, duration or type of diabetes mellitus. Accordingly, the search for genetic markers, neuroimmunological indicators, the relationship with clinical and neurophysiological indicators in children with DM is relevant, can help to identify a group of children and adolescents at risk for the development of DN, prevention and therapy in the early stages of the complication (5, 8, 4). Purpose of the work. To study the state of cerebral and ciliary neurophilic factors in children and adolescents with diabetic neuropathy.

Material and methods of research. Children and adolescents from 8 to 18 years of age with diabetes mellitus, regardless of type, were included in the study. The control group was children and adolescents of identical age without diabetes mellitus - 15. In addition, children and adolescents with polyradiculoneuritis of inflammatory genesis - 20 were included in the study. Children and adolescents with diabetes mellitus out of 100 children only patients with sensorimotor polyneuropathy - 42, among them patients with subclinical form - 19, clinical form - 23 were included in the study. The study was conducted for the period 2020-2022, on the basis of the endocrinological hospital of Samarkand and on the basis of 1-clinic of the SamMU Department of Paediatric Neurology. All children underwent standard clinical and neurological

examination, ENMG instrumental method of investigation, TSS (general scale of neurological symptoms modified for the age of patients, if necessary) and NDS (neuropathic dysfunctional score) functional scales were studied. Laboratory analysis, taking into account the objective, involved the determination of ciliary and cerebral neurotrophic factor. Statistical data were processed on an individual computer using standard Student's criteria.

Study Results. Researchers in many scientific studies have found that neurotrophic factor plays an important role in the protection and support of the peripheral nervous system, as it contributes to the strengthening of myelin by Schwann cells. And since schwann cells have a powerful effect on axons, it is suspected that it is the deficiency of neurotrophic factor levels that contributes to the deterioration and progression of peripheral nerve damage in diabetes. Both ciliary (CF) and brain-derived (BF) neurotrophic factors have been studied in the groups described. CF (ciliary) factor in DiP on the average, according to the results showed 21,0 pkg/ml, in healthy children this index was 10,9 pkg/ml, but in children with PVH corresponded to 19,5 pkg/ml, where p=0,001. At the same time brain-derived neurotrophic factor (BF) in DiP with SMP is equal to 9578 pkg/ml on average, in healthy children the results are close to the norm 6233 µg/ml, and the most interesting thing is that in children with PVH were changed and corresponded to 9379 pkg/ml, where in significance p=0,0001. When analysing the neurotrophic factors in D and P depending on the type of DM, it turned out that the factor was significantly higher in DP children with type 2 DM. So in DP with SMP with DM type 1 BF is equal to 9052 pkg/ml on average, and type 2 on average 9574 pkg/ml, where p=0,001. At the same time, in the subclinical stage, the BF figures were on average between 8778 pkg/ml and in the clinical stage 9400 pkg/ml, where p=0.0001. As for the changes of cerebral neurotrophic factor depending on the duration of the disease, more than 10 years there is a slight decline to decrease and is equal to 9393 pkg/ml, most likely this fact is associated with adaptation to the disease over a sufficiently long period. But, what cannot be said about ciliary neurotrophic factor, where on a long period of the disease CF reacts by increase of indicators, on 10%, that had a limit in average 30,9 pkg/ml, p=0,0001. Again, the statistical correlation required to control the relationship of neurotrophic factor, clinic and instrumental data, revealed a close relationship of the studied indicators, where CF and BF, R=0.76, p=0.002. So, the results obtained confirm the relationship and direction in the same mode, which unites them as the pathogenetic nature of the disorder. As in previous studies, interest in the change depending on the duration of the disease, the level of glycated haemoglobin indicator, on the form of the disease. In patients where the duration of the disease did not exceed 10 years, a rise in the level of cerebral neurotrophic factor up to 9680 pkg/ml was naturally observed, and when the disease duration exceeded the limit of 10 years (12-15 years), a characteristic decrease in BF up to 9250 was observed. At the same time, the level of ciliary neurotrophic was statistically consistently high in patients with both 5 years and more than 10 years of diabetes mellitus. Depending on the form of the disease, the following indices were found, in the subclinical form detected concentrations of BF within 9570 and SF 25.8 pkg/ml, that is, on the face of the increase in the figures, which suggests the likelihood of an early reaction of Schwann cell factor in response to the initial stage of axonopathy, for the regeneration of peripheral nerve damage. Of course, cerebral neurotrophic factor also responds to the level of high (compared to the control) glycated haemoglobin, the higher the blood sugar, the higher the BF; But ciliary neurotrophic factor is elevated even at relatively stable (insignificantly high) levels of glycated haemoglobin, HvA1 and SF, R=-0.26, p=0.04. Interesting was the fact that in patients where electroneuromyography parameters were not changed, there was a change in SF, which gave reason to estimate these patients as having a subclinical form of the disease, respectively, the index of SF can be considered as a test for prognosis and determination of complications of DM in children and adolescents at an early stage. In the examined patients with clinical form of the disease older than 15 years, with a long history of the disease, high BF=9895 pkg/ml, and low SF=19.9 pkg/ml were characteristic. The correlation between this category of patients and instrumental changes on ENMG revealed a very low M-response, <0.55 mv, and on SRV, <39m/s, which gives a difference between the norm of

half. So, there is progression and diminishing process. Correlation analysis with electroneuromyography parameters in the subclinical stage indicates increased BF and unchanged ENMG parameters, i.e. the level of cerebral neurotrophic factor can serve as an early marker for diabetic sensorimotor polyneuropathy. The level of ciliary neurotrophic factor in comparison with ENMG indices in subclinical stage were identical, CF increased, without changes in myographic indices, which is also the basis for carrying out these analyses in diabetic patients with DM for diagnostics of early forms of sensorimotor polyneuropathy. And the related concentration of ciliary and brain neurotrophic factor within the correlation direct index, where p=0,0002, speaks about the supposed disturbance from the side of peripheral nervous system. Not stopping there, a curve of ciliary neurotrophic change was drawn up, in order to determine the development of severity into 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 ciliary neurotrophic factor should not exceed 6 pkg/ml. in correlation analysis with ENMG, which is considered indicative in the clinical stage. The study of ciliary neurotrophic factor is currently necessary to confirm the diagnosis, but also to determine the long-term prognosis and, consequently, to determine the treatment tactics. In order to obtain a more complete model of interaction of neurotrophic factors with the results of other indicators depending on the form of the disease, we decided to correlate them with SR 21,0 19,5 10,9 0,001BF 9578 9379 6233 0,0001Average BF8778 9400 0,0001testing by scales. The results of the conducted correlation analysis on the TSS scale (general scale of neurological symptoms), where the indices were in the range from 3.5 to 7.5 points (average 5.5), with the indices of neurotrophic factor, in the subclinical form of SMP, correlation by the degree of prognosis, that is, in the absence of the possibility to use laboratory tests, with the same success indices on the scales, can serve as a productive prognosis in the diagnosis. But only in the aggregate study of indicators of several scales, for example, the use of the scale N D S (neuropathic dysfunctional score), which showed the reliability of sensorimotor disorders from the degree of severity of the disease and was within the range of 10 to 14 points. The severity of diabetic polyneuropathy according to the NDS scale had statistically significant correlations with neurotrophic factors, which can also be used as one of the evidentiary indicators 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 can not always correctly and clearly assess the level of the lesion, respectively, questionnaires on the scales, and electroneuromyographic examination can not be definitive in making a diagnosis, its form and severity, so the laboratory character of recognition is maximally indicative.

CONCLUSIONS:

1. Correlation analysis with electroneuromyography in the subclinical stage indicates elevated BF and unchanged ENMG values, i.e. the level of brain-derived neurotrophic factor can serve as an early marker for diabetic sensorimotor polyneuropathy.

2. The severity of diabetic polyneuropathy according to the NDS scale had statistically significant correlations with neurotrophic factors, which can also be used as one of the evidentiary indicators in this category of patients.

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