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NEW METHODS FOR THE TREATMENT OF DIABETIC NEUROPATHIES IN YOUNG CHILDREN

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Abstract: The article is devoted to new methods of treatment of diabetic neuropathies in young children. The results are based on the reduction of complications of the disease and return of children to a healthy life. Diagnostics and optimisation of the disease treatment allowed to create an algorithm of the disease course.

Key words: Neuropathy, demyelination, axonopathy, ciliary factor, brain neurotrophic factor, myelin.

Introduction. According to the World Health Organisation, diabetes mellitus (DM) is a worldwide epidemic. The insidious, slowly progressive increase in malignancy makes it difficult to determine accurate prevalence rates that reflect the risk of complications (2,6). To date, there are a large number of hypotheses for the mechanism of neurological complications, allowing the term uncomplicated diabetes to be used rather than a manifestation of nervous system disease (7,10). Undoubtedly, the main component of metabolic diseases is represented in the form of diabetic neuropathy. One of the points considered in the pathogenesis is the impairment of glucose to sorbitol conversion up to 10%, in which aldose reductase is converted to sorbitol by non-phosphoric glucose and eventually sorbitol is converted to fructose (1,8). This entire excretion pathway leads to accumulation and elevation of blood glucose levels. Glucose increases circulating phosphatidylinositol and limits axonal activity, conduction velocity is dramatically reduced and axonopathy occurs (5,9). Aldose reductase is activated, suppresses NADPH and reduces glutathione (antioxidant) formation, in parallel free radicals are reduced and oxidative stress occurs (9,10).

A number of authors have studied in detail the histological changes in diabetic neuropathies for 100 years and confidently speak about the beginning of degeneration of the myelin sheath in the early stages of the disease. The same destructive processes occur in schwann cells, leading to demyelination of nerve fibres (3). Pathologists have examined schwann cells at different levels (motor, sensory) in patients who died of QD and found significant changes in the cytoplasmic level of schwann cells as well as in unmyelinated fibres (2,5,6).

Purpose: To optimise the treatment of diabetic neuropathies in children.

Materials and methods of the study. 100 children with diabetic neuropathy aged 3 to 17 years were included in the study. Of them 45 - children with subclinical form of the disease (DNS), 55 - children with clinical form (DNS). According to clinical symptomatology: sensorimotor polyneuropathy (SMN) - 45 children, radiculopathy (R) - 27 children, plexonopathy (P) - 13 children, peripheral mononeuropathy (PM) - 15 children. All patients were divided into groups to study the efficacy of the proposed pathogenetic treatment based on a comprehensive examination (clinical and neurological examination, functional scales, ENMG, laboratory data on neurotrophic factors). The process of control of treatment efficacy was 3 months, since the process of diabetic neuropathy itself depends on the duration of the underlying disease. The treatment of the examined patients was carried out with parental consent, taking into account an additional conversation with parents about the significance of treatment methods, and parents were given the opportunity to choose the recommended therapy.

As a result, three groups were formed, one of which was monitored only according to the indicators specified in the protocol of outpatient treatment without additional treatment; such children and adolescents (group 3) were 23 out of 100 examined. Group 2 (36 patients) received magnetotherapy in combination with drug treatment (BTL 5000 2014, Germany) for 10 sessions every 2 months, for a total of 3 courses. Biowen, immunoglobulins class G, Biowen mono 0.4 g/kg per day for 5-7 days, total 2 courses every 3 months. Children of group 1 (38) received immunomodulatory therapy together with the treatment received in group 2, children over 10 years old were administered immunomodulatory cyclophosphane in the initial dose of 2mg/kg, after 1.5 months the dose was reduced. The period of administration is up to 3 months. Glycaemia level was monitored daily (results were recorded in individual glucometers). At the end of the observation period (6 months) the patients were re-examined. Statistical data were processed on a personal computer according to standard criteria of requirements.

Results of the study. At the initial examination the main symptom of diabetic neuropathy was pain and decreased reflexes. Pain was characterised by a variety of symptoms: numbness, paresthesias, burning, specific in quality and quantity. According to statistical calculations, a significant difference in scores was found before treatment and after the recommended treatment. Thus, there is a significant difference in the nature of scores before treatment and after treatment for complaints: before treatment 2.7±2.2, after 6 months in group 1 0.4±1.2; 0.6±1.5 in group 2; in group 3 (control) 2.3±2.0 (p=0.03). Changes in the TSS questionnaire in the examination groups revealed a significant decrease in group 1; the mean TSS score before treatment was 6.6±7.0; After treatment, it decreased to 2.28±2.1 in group 1; 2.8±2.4 in group 2; 4.6±5.3 in group 3 (p=0.02). Baseline versus post-treatment status of patients on the NDS scale averaged 4.6±3.3 before treatment, 3.8±1.5 after treatment in group 1; 4.2±1.9 in group 2; In group 3 control group (number of groups) it decreased to 4.9±2.5 (p=0.7). The assessment of sensory symptom scores conducted in parallel on the NDS scale (temperature, tactility and vibration) had a significant decrease. Initially the scores averaged 6.0±1.5, after treatment they decreased to 2.6±2.0 in group 1; 3.3±2.1 in group 2; 4.7±2.5 in group 3 (p=0.005).

The results of dynamic parameters of electroneuromyography in the study in three groups were difficult due to their diversity, the number of different clinical groups of nerves; in this respect, n. tibiabis turned out to be the most common, on which basis the study was based on the conduction velocity of these nerve fibres. Thus, the mean values before treatment were 32.6±2.0 m/s, and after treatment there was an increase in conduction velocity of 42.2±3.2 m/s in group 1, group 2 40.1±3.0 m/s, group 3 33.9±2.9 (p=0.033), a slight improvement was maintained. There was also an improvement in M-response amplitude before treatment, which after treatment in group 1 was 6.4±2.9 (p=0.033). Regarding SRV dynamics parameters before treatment, the mean values after treatment were 35.9NDS±7.3 m/s in group 1, 34.1±6.5 m/s in group 2; In group 3 it was 32.93±5.8 m/s (p=0.033) respectively. Thus, there is a clear picture of better dynamics in the main groups, especially in group 1, where patients received magnetotherapy + aziotioprine (Table 1).

Table 1. Pre and post treatment indications of DN according to complaints, clinical features.

Indications	1 group		2 group		3 group	
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment
Complaints: pain, insomnia, redness, paresthesia	2,6±2,3	0,3±1,3	2,7±2,5	0,4±1,6	2,3±2,0	2,1±2,0
TSS	6,8±8,0	2,24±2,0	6,8±8,1	2,7±2,56	6,8±8,0	4,3±5,5
NDS	4,8±3,2	3,7±1,5	4,7±3,0	4,0±1,9	4,8±3,3	4,6±2,6
Sensitivity	6,0±1,5	2,5±2,0	6,0±1,7	3,2±2,0	6,0±1,7	4,5±2,5

Table 2. ENMG parameters (m/s) in dynamically examined patients before and after treatment

Indicators	1 group		2 group		3 group		P
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	After treatment	
ENMG	32,6±2,0	42,2±3,2	33,0±2,0	40,1±3,0	32,9±1,9	33,9±2,9	0,033
M-response	6,4±2,9	8,9±4,0	6,5±3,0	7,0±3,8	6,4±2,5	6,8±3,0	0,033
SRV	31,72±1,0	35,9±7,3	32,0±1,0	34,1±6,5	31,8±1,0	32,93±5,8	0,033

Laboratory studies have allowed enough reflection on the importance of the dynamics of diabetic neuropathy in children and adolescents, and yet there are indicators that should be considered as more prognostic signs. For example, ciliary neurotrophic factor (CF), its decrease from normal values indicates the severity of the complication of diabetes mellitus, that is, diabetic neuropathy. In the literature, CF is used to treat cholinergic neurons as a trophic factor. As mentioned above, baseline values of CF have low figures confirming clinical signs of DN, on average up to 5.3 pg/ml. Against the background of treatment there is a statistically significant increase in the level of ciliary neurotrophic factor. Moreover, in group 1 the indices increased twice as compared to the initial values and approached the standard values, on average 11.5 pg/ml (in the norm 12.2 pg/ml). In group 2, this indicator increased one and a half times and was 7.5 pg/ml. When analysing the CP in group 3, the indices changed insignificantly, where no additional treatment was performed, which amounted to 5.0 pg/ml (p=0.01).

Table 3. Ciliary neurotrophic factor values in groups before and after treatment (ng/ml)

Indications	1 group		2 group		3 group		p
	Before treatment	After treatment	Before treatment	After treatment	Before treatment	Indications	
Ciliary neurotrophic factor (CF)	=5,3	=11,5	=5,3	=7,5	=5,3	=5,0	0,01

Conclusions: These indices confirmed the proposal of proper use of azathioprine and bioven drugs, the action of this neurotropic mechanism regardless of the duration of DM, the level of glycated haemoglobin subclinical, with the addition of MAP with DN indicates the use of magnetotherapy. Thus, in patients who did not receive additional treatment, no significant changes in the concentration of ciliary neurotrophic factor from the baseline level were found.

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