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NEUROLOGICAL COMPLICATIONS AND PARACLINICAL INDICATORS IN DIABETES MELLITUS

Abdukadirova D.T., Mukarramov U.M.

Andijan State Medical Institute

Neurology department

Andijan, Republic of Uzbekistan

Abstract: This research work include relevant information about different results those taken from Electromyographic exam in patients who are suffering from type 2 Diabetes mellitus with different body mass indexes. That may help us to explain the negative impact of the obesity in the development of neurological complications in Diabetic patients.

Key words: Electromyographic exam, type 2 Diabetes mellitus, body mass index, obesity, neurological complications.

Relevance

It is true that, despite developments in diagnosis and treatment, complications of diabetes mellitus (DM) still cause a major concern for patients and their families. Damage to the blood supply can lead to blindness, kidney failure and limb amputation, myocardial infarction and stroke in patients with diabetes occur at a higher frequency than in the general population and are the main cause of death in patients with this disease. The problem of damage to the nervous system in diabetes mellitus also leaves many unanswered questions. Damage to the peripheral part of the nervous system in the syndrome of insulin resistance is associated with the presence of DM [1, 8]. Although scientists provided information the role of obesity in the development of neurological disorders, information about the leading role of increased body mass index remains controversial [7].

The choice of medications used in the treatment of diseases of the nervous system pathways is usually limited to the use of alpha-lipoic acid, Miltgamma and anticholinesterase drugs. In some cases, with the undoubted autoimmune nature of the disease, glucocorticosteroid and immunosuppressive drugs, as well as immunoglobulins and plasmapheresis, are successfully used. In this regard, the search for new drugs that have broad potential for use in the treatment of various forms of pathologies of the conduction neuromotor apparatus is very relevant (1, 2).The Ipidocrine molecule (mediatorn) is a non-selective inhibitor of acetylcholinesterase and butyrylcholinesterase, which has the effects of a blocker of membrane potassium channels and indirectly increases the rate of entry of calcium ions into the axon terminal.The latter property of the drug further enhances acetylcholinergic transmission, as it lengthens the period of excitation in the presynaptic fiber and, accordingly, the time of release of acetylcholine into the synaptic cleft. The blockade of potassium permeability of the membrane favorably distinguishes Mediatorn from classical acetylcholinesterase prepatates, making it a “unique stimulator” of impulse conduction in the nervous system, since this pharmacological effect helps to accelerate impulse transmission along the nerve fiber and facilitates its conduction in synapses of all types (regardless of the

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type of mediators). The ipidacrine molecule (Mediatorn) penetrates the blood-brain barrier, stimulates central cholinergic transmission, has an activating effect on the central nervous system in combination with some sedative effects, and improves cognitive functions, including learning and memory.

Research Material

The study was conducted on the basis of the clinic of the Andijan State Medical Institute (I, II and III neurological departments) and the Regional Endocrinological Dispensary. The inclusion criteria for patients in the study were the presence of verified type II DM (DM-2); disease experience of at least 5 years; age from 45 to 65 years; absence of focal brain damage according to MRI; signing of voluntary informed consent to participate in the study. The exclusion criteria were the presence of severe or unstable comorbid somatic pathology, acute cerebrovascular accident, myocardial infarction, alcohol disease, substance abuse.20 patients diagnosed with type 2 diabetes mellitus (DM-2), 8 (40%) men and 12 (60%) women, aged 45 to 65 years, were examined, the average age of patients was 52.3+12,9 years. During the study, the patients were divided into two groups. The first group consisted of 5 (25%) patients who did not have increased body weight (BMI < 25), for this group the average BMI was 19.2+5.8 and the HbA1C level was 8.8+0.4%. The second group included 15 (75%) patients whose body weight was above normal (BMI>25). In this group, the average BMI was 31.8+7.3, and the HbA1C level was 9.2+0.8%.

Analyzing the data of patients selected for the study, we can draw the following conclusions: there were more women among patients - the gender index was 1.5 in favor of the female; there were a significant number of patients with increased body weight (BMI> 25.0) - 12 people (75%).During the study, patients in the main group were prescribed the ipidacrine molecule (Mediatorn) according to the following scheme: injections of a 1.5% solution, 1.0 ml per day for 10 days, then taken orally at a dose of 20 mg 2 times a day for three months. The control group did not receive complex treatment. In the dynamics of treatment, the clinical and neurological status was assessed, taking into account the degree of changes in the sensorimotor sphere of both the central and peripheral nervous systems.

The effectiveness of the therapy on cognitive functions was assessed using scales such as: 1. Mini Mental State Examination (MMSE); 2. Mattis Dementia Rating scale (MDRS); 3. Neuropsychological tests included a battery of frontal tests, tests of drawing a clock, memorizing and reproducing 10 words, and repeating numbers forward and backward. The following criteria were used as criteria for the effectiveness of Neuromedin in DPN: 1. assessment of negative neuropathic symptoms (sensorimotor) using a scale of neuropathic disorders in the legs (Neuropathy Impairment Score Low Limbs - NIS-LL); 2. assessment of positive neuropathic symptoms (patient complaints) and stimulus-dependent pain using a modified neuropathic symptom scale (Neuropathy Total Symptom Score - NTSS-9); 3. assessment of the functional state of the peripheral nerves of the legs based on the results of stimulation EMG. All data obtained were subjected to statistical processing.

Research Methods

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All patients underwent a standard clinical and neurological examination (analysis of patient complaints, anamnesis of life and anamnesis of the disease, an objective examination, including a study of the neurological status) and a physical examination. Electroneuromyographic parameters were recorded on an MBN neuromyograph device Electroneuromygraphic (ENMG) study carried out with the aim of:

1. Objectification of damage to motor and sensory fibers of peripheral nerves.

2. Identifying the nature (demyelinating, axonal) and the degree of nerve damage.

3. Studying the relationship between clinical and electrophysiological manifestations of DN

Research results

The ENMG study made it possible to verify signs of symmetric peripheral axonal-demyelinating damage to nerve fibers in patients with diabetic polyneuropathy in general. A comparative analysis of neurophysiological parameters in groups with clinically manifested neuropathy did not reveal statistical differences, however, nerve conduction disorders in patients with a severe stage significantly exceeded. The average temperature of the extremity, recorded using a thermal sensor when assessing nerve conduction, did not differ significantly in all patients. In group I it was 29.31±3.120 C, in group II it was 27.45±1.640C. Patients of group II showed signs of severe axonal dysfunction, represented by a decrease in the amplitude of sensory and motor responses by more than 50%: the average value of the C-response of the sural nerve, which amounted to 2.37 ± 0.41 mV, was significantly lower than the corresponding indicator of patients in group I - 4.57 ± 2.36. The amplitude of the motor response, on average, was reduced throughout, to a greater extent in the distal sections, which indicates axonal damage of the polyneuritic type. In group II, a slowdown in the spread of excitation along the sural nerve was also revealed, and the speed of impulse conduction along the peroneal nerve was reduced.

The average values of the M-response of the peroneal nerve in patients of group I were 2.78 ± 1.65 mV at the level of the ankle, under the head of the fibula - 2.84 ± 1.37 mV, in the popliteal fossa - 2.77 ± 1.62 mV, in patients of group II, these indicators were significantly lower and amounted to 1.05±0.83; 0.95±0.72; 1.07±0.53, respectively. Secondary demyelinating changes, represented by an increase in the latency of the sensory, motor response and a decrease in CRV, also occurred in patients with DPN. In all groups, there is a slight increase in the latency of the C-response, no significant intergroup differences in this indicator were found: in group I -3.69±1.23 ms, in group II - 4.76±1.57 ms. This indicates a higher localization of the demyelinating process in patients of group II.

In the study of the peripheral nerves of the arms and legs in group II, signs of the demyelinating nature of the lesion throughout the nerve fiber were revealed in the form of a decrease in CRV in the distal sections of the motor and sensory nerves, an increase in the distal and residual latency, an increase in the minimum latency of the F-wave, a decrease in the minimum and maximum NRT F-waves. In the most distal parts of the nerves of the legs, signs of demyelination were also revealed, as evidenced by an increase in the average values of distal and residual latency: when examining the median nerve, the distal latency was 2.7±1.2 ms; in the study of the tibial nerve, the residual latency was 4.3 ± 0.2 ms. When

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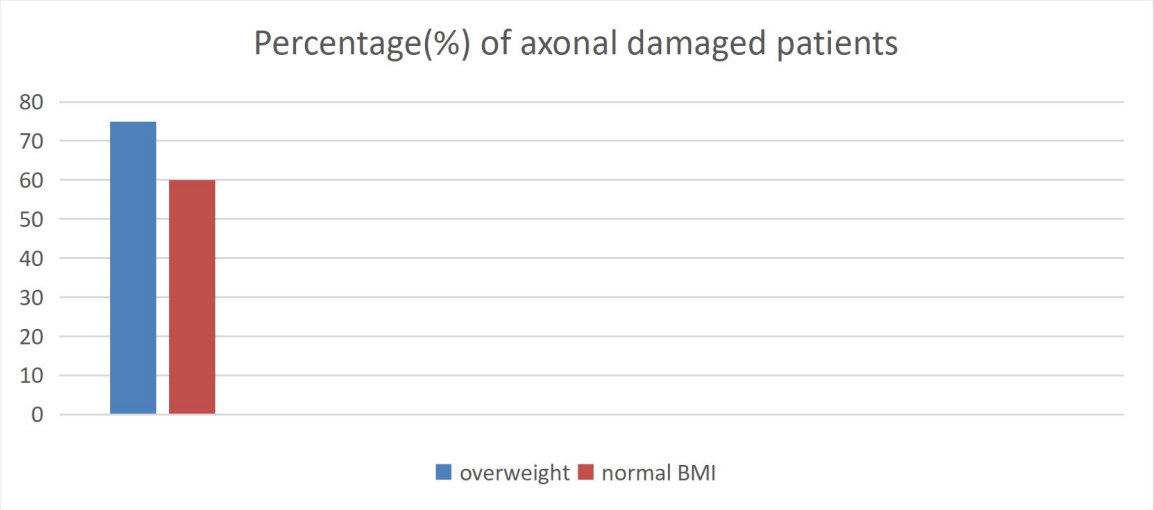
comparing EMG parameters of the nerves of the upper and lower extremities, a significantly higher distal and residual latency was revealed during stimulation of the nerves of the legs compared to the median nerve. When comparing EMG - indicators of the median nerve in groups in group II, lower values of SRV for sensory and motor fibers, as well as higher indicators of residual latency ($p<0.05$) were revealed. F-wave prolapse in patients in group I, unlike group II, was much less common: during stimulation of the median nerve in group II, F-wave prolapse was observed in 50% of cases, and in group I - in 40%. When examining the nerves of the legs in type II group, lower values of CRV and M-response amplitude were revealed compared to group I ($p<0.05$).When studying the relationship between EMG parameters and the clinical picture of DM, the following were revealed: 1) a negative correlation between the duration of the disease and the amplitude of the M-response ($r = -0.4$; $p < 0.05$), indicating more pronounced axonal damage with an increase in the duration of the disease; 2) a positive correlation between the strength of the distal muscles and the amplitude of the M-response of the peroneal nerve ($r = -0.48$; $p < 0.05$), indicating the effect of axonal degeneration on the severity of neuropathy; 3) a negative correlation between the number of F-waves falling out during stimulation of the sural nerve and distal strength in the legs ($r = -0.52$; $p < 0.05$), which indicates the possible presence of impaired impulse conduction and the development of distal weakness.

Conclusion1. EMG study revealed the demyelinating nature of the lesion in patients with type 2 diabetes. The nature of the demyelinating process in the subgroups was somewhat different: In a patient with type 2 diabetes and increased BMI, along with signs of diffuse demyelination in the form of a decrease in CRV, an increase in distal and residual latencies, F-wave latency, signs of local demyelination, as well as F-wave prolapses, were revealed, which may indicate the presence of a lesion in the most proximal sections of the nerve fiber. Comparison of CRV and residual latency in a patient with type 2 diabetes and increased BMI revealed statistically significant lower values, which indicates a greater damage to the myelin sheath compared to patients with type 2 diabetes with normal body weight. 2.Signs of the axonal nature of the lesion during stimulation of the nerves of the lower extremities in a patient with type 2 diabetes and increased BMI were detected in 75% of cases, and in patients with type 2 diabetes with normal body weight - in 60% of cases.



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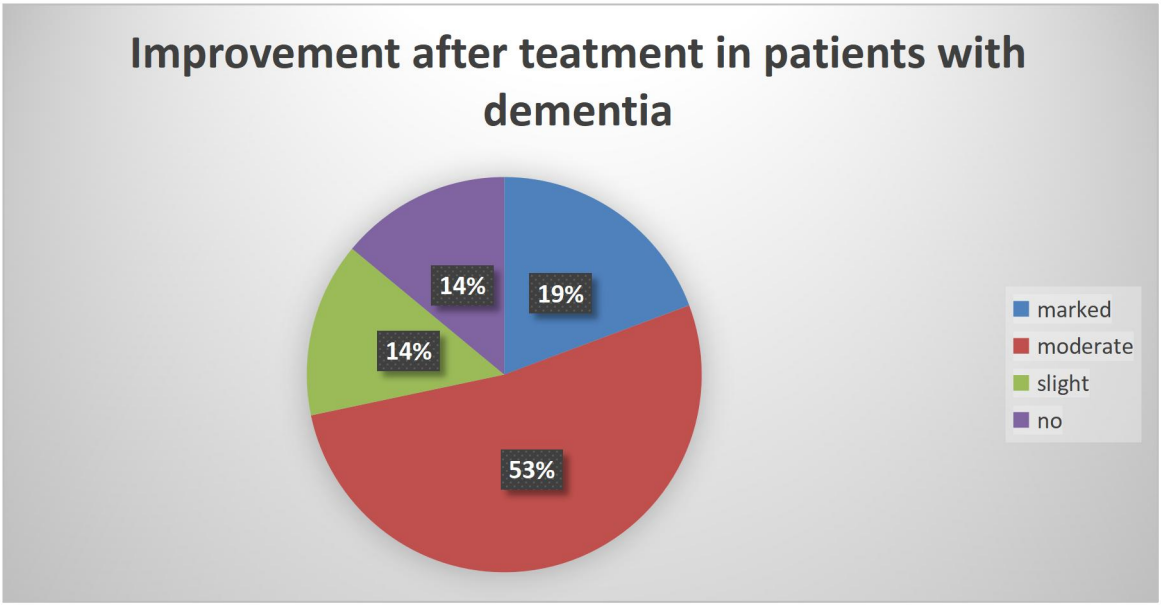
3.A patient with type 2 diabetes and elevated BMI also showed statistically significantly lower M-response amplitudes compared to patients with type 2 diabetes with normal body weight.

In the process of complex therapy, we noted positive dynamics of cognitive and mental functions, along with positive changes in the peripheral nervous system.

Results of a study on diabetic cognitive dysfunction.

The therapy provided clinically significant improvement in both patients with dementia and patients with mild cognitive impairment. In the dynamics of treatment of patients with dementia, we observed a marked improvement in 19.3% of patients, a moderate improvement in 52.4%, a slight improvement in 14.3% and no changes in 14%.



Improvement in cognitive functions of varying degrees of severity was noted in the dynamics of treatment in the examined patients. For example, 13.5% experienced a sharp improvement in cognitive function; during treatment, these patients experienced changes from “moderate cognitive impairment” to “mild cognitive impairment.” Significant changes in cognitive functions were observed in the first month of therapy, the improvement was maintained during further observation. During mediator therapy, when assessing the dynamics of cognitive functions, we obtained the most pronounced and significant changes in indicators of mnestic function, such as: memory, attention, concentration, mental activity, abstract thinking and constructive abilities. A positive effect was observed in the form of easier reproduction of “old” knowledge - the elimination of selective retrograde amnesia, easier memorization of current events, easier abstraction and thinking, and an increase in the volume of auditory-verbal and visual memory. The following indicators were adopted as criteria for effectiveness: improvement in memory and other cognitive functions (48.7%), reduction in the severity of neuropsychiatric symptoms (64%), increase in the length of time of relative functional independence of the patient (63%), improvement in the patient’s quality of life (58%), reduction in the burden on caregivers (77%).

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The above indicates the beneficial effect of the drug on the primary mechanisms of remembering and reproducing information, the violation of which is one of the early and important manifestations of dementia.

Results of a study on diabetic polyneuropathy.

A decrease in neurological deficits as assessed using the NIS-LL scale shows that treatment with a mediator leads to an improvement in the functions of peripheral nerves, and the dynamics on the NTSS-9 scale reflects this indicator. This fact is also confirmed by an increase in the amplitude of the M-response upon stimulation of the peroneal nerve against the background of complex therapy.

In the patients studied, we also observed a regression of pain by 54.8%, paresthesia by 61.2%, and cramps by 80.2%. This was expressed by the following indicators: on the NTSS-9 scale, the sum of points before and after treatment in the main group was 2.68±0.59 points, and in the control group – 1.45±0.53 points ($p<0.05$). In the main group, the severity of all sensory symptoms decreased, most significantly - paresthesia (3.66 - 1.39, respectively), cramps (3.82 - 2.05), vegetative pain (3.30 - 2.50). The difference in the total scores on the NIS-LL scale before and after treatment was 1.12±0.41 points versus 0.09±0.20, respectively. The Ipidacrine molecule, by lengthening the period of repolarization of the axon membrane, is able to block ectopic foci of excitation and ephaptic transmission of excitation, which apparently are the cause of the formation of pain, paresthesia and cramps.

Conclusion

The study noted that the main mechanism of action of the ipidacrine (mediatorn) molecule contributes to a significant improvement in the processes of neuroplasticity in the peripheral and central nervous system. This relates to sprouting processes, effects on ion channels, improvement of neurotransmission, primarily in cholinergic synapses. A study conducted on the effectiveness of Mediatorn showed its powerful potential as a pharmacological neurorehabilitation drug - an original modulator of neuroplasticity.

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