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## TREATMENT OF DIABETIC POLYNEUROPATHY

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### ABSTRACT

The authors have studied the effect of mildronat and thiotriazolin on the processes of lipid peroxidation, the oxidative modification of proteins and the state of the blood antioxidant system 3 and 6 months following a course of multimodality treatment in patients with diabetes mellitus and diabetic polyneuropathy.

**Keywords:** diabetic polyneuropathy, diabetes.

**Introduction.** There are nearly 1 million diabetic patients in Ukraine, and it is believed that approximately the same number has undiagnosed DM. Thus, the real number of cases is around 2-2.5 million of people [3, 4]. Over the past 10 years, the incidence of diabetes has increased more than 1.5 times, and mortality has increased 2 times [5]. The economic and social damage caused by this disease is enormous because of its prevalence and disability it leads to. One of the most common and the most widespread neurological complications of the diabetes mellitus (DM) is a diabetic polyneuropathy (DPN) (the incidence according to various literary sources ranges from 20% to 93% depending on the type of diabetes and diagnostic methods) [1, 2]. It is one of the most common diseases, and it remains one of the most difficult health and social problems.

**The aim of the study.** To investigate the effect of mildronat and thiotriazolin on the processes of lipid peroxidation (LP), proteins oxidative modification and the state of the antioxidant system of blood 3 and 6 months after multimodality treatment in diabetic patients with DPN.

**Objectives of the study.** To study the effect of the mildronat and thiotriazolin on the processes of lipid peroxidation, proteins oxidative modification and the state of the blood antioxidant system 3 and 6 months after multimodality treatment in diabetic patients with DPN.

**Materials and methods.** We examined 32 patients with diabetes of type II, who were hospitalized in Chernivtsi Regional Clinical Endocrinology Dispensary. Among the patients there were 20 women and 12 men, the age of the patients ranged from 36 to 65 years old. Moderate diabetes was observed in 30 patients whereas 2 patients were in critical condition. 9 patients were in a position to compensate for the disease, 23 had subcompensation. Patients were divided into 2 groups. Group I consisted of patients receiving basic therapy; it included diet № 9, 5 mg of maninil twice a day or insulin (2/3 of daily dose in the morning and 1/3 of dose in the evening, 0.7 - 1.0 U / kg of body weight), pentoxifylline taken intravenously 5 ml per 250 ml of the isotonic sodium chloride, vitamins B6, B12 (14 patients); Group II consisted of patients that along with basic treatment received TTZ (2 ml of intramuscularly 2.5%

solution 1 time per day for two weeks) and MD (5 ml of bolus intravenous solution 10% 1 time per day) (18 patients). The control group comprised 20 almost healthy individuals.

### Research results discussion

The evolution of lipid peroxidation and protein as well as the state of the blood antioxidant system 3 and 6 months after basic treatment in patients with diabetic polyneuropathy is shown in Table 1. Patients with DPN who took basic treatment have the activation of lipid peroxidation and protein and inhibition of the state the blood antioxidant system 3 months after treatment which is shown by reduction of the glutathione content, HS-groups, increasing activity of ceruloplasmin, malonic aldehyde content, decreased activity of catalase, G-6-PD and an increase in content of ketones and aldehydes of neutral character ( $\lambda$  370) and main character ( $\lambda$  430). 6 months after treatment, these figures hardly differed from the corresponding parameters the patients had shown before taking treatment.

The evolution of lipid peroxidation and protein and the state of the blood antioxidant system 3 and 6 months after the addition of MD and TTZ in patients with DPN is shown in Table 2. 3 months after treatment with the addition of MD and TTZ in patients with DPN there was no significant alteration of lipid peroxidation and protein indicators and the state of the antioxidant system of the blood in comparison with the patients after the discharge. Thus, there was only a tendency for increasing the activity of ceruloplasmin, content of malonic aldehyde, a slight decrease of glutathione, HS-groups, catalase activity, G-6-FDG and increasing of ketones and aldehydes of neutral character ( $\lambda$  370) and the main character ( $\lambda$  430) in comparison with the patients after discharge. 6 months after treatment with simultaneous use of MD and TTZ there was an increase in activity of ceruloplasmin by 59.5%, malonic aldehyde content by 20.3%, a decrease of glutathione content by 37.8%, HS-groups by 24.5 %, catalase activity reduction by 18.8%, G-6-FDG by 20.5% and an increase of ketones and aldehydes of neutral character ( $\lambda$  370) by 66.1% and ketones and aldehydes of the main character ( $\lambda$  430) is by 48.2%.

**Conclusions**

1. 3 months after basic therapy there is activation of lipid peroxidation and protein and inhibition of the state of the blood antioxidant system. 6 months after treatment, these figures hardly differ from the corresponding parameters the patients had before taking the treatment.

2. When taking basic treatment accompanied by MD and TTZ, there is activation of lipid peroxidation and protein and inhibition of the state of the blood antioxidant system only 6 months after the therapy, indicating the need to go through re-treatment.

Further research in this area will significantly improve the treatment of diabetes patients complicated by neuropathy.

Table 1

**The evolution of lipid peroxidation and protein and the state of blood antioxidant system 3 and 6 months after the basic treatment in diabetic polyneuropathy patients (M ± m)**

Indexes	The Control	Before treatment	In 2 weeks	In 3 months	In 6 months
The activity of ceruloplasmin (mg / l)	167 ± 8,2	317 ± 7,1 (p<0,01)	305 ± 9,3 (p>0,05)	313 ± 8,7 (p>0,05)	322 ± 8,9 (p>0,05)
The content of reduced glutathione (mmol / mL)	2,02 ± 0,08	0,86 ± 0,06 (p<0,01)	0,96 ± 0,07 (p>0,05)	0,92 ± 0,07 (p>0,05)	0,89 ± 0,07 (p>0,05)
The content of HS-groups (mmol / 1 ml cr. weight)	2,59 ± 0,08	1,61 ± 0,05 (p<0,01)	1,68 ± 0,04 (p>0,05)	1,65 ± 0,06 (p>0,05)	1,62 ± 0,08 (p>0,05)
The content of malonic aldehyde (mmol / L)	20,4 ± 0,43	33,1 ± 0,51 (p<0,01)	32,7 ± 1,2 (p>0,05)	32,9 ± 1,4 (p>0,05)	33,8 ± 1,7 (p>0,05)
The activity of catalase (Mkkat / g of protein)	5,3 ± 0,3	3,6 ± 0,2 (p<0,01)	3,8 ± 0,2 (p>0,05)	3,7 ± 1,2 (p>0,05)	3,6 ± 1,4 (p>0,05)
The activity of G-6-FDG (In mmol / min (g Hb)	4,21 ± 0,11	2,76 ± 0,23 (p<0,01)	2,88 ± 0,12 (p>0,05)	2,85 ± 0,13 (p>0,05)	2,78 ± 0,14 (p>0,05)
ketones and aldehydes of neutral character (λ 370) (mmol / g protein)	1,51 ± 0,12	3,26 ± 0,12 (p<0,01)	2,89 ± 0,15 (p>0,05)	2,99 ± 0,14 (p>0,05)	3,23 ± 0,17 (p>0,05)
ketones and aldehydes of main character (λ 430)	19,48 ± 2,6	41,88 ± 2,8 (p<0,01)	38,43 ± 2,1 (p>0,05)	39,67 ± 2,9 (p>0,05)	41,45 ± 2,3 (p>0,05)

Note: p - the probability is compared with patients before treatment;

Table 2

**The evolution of lipid peroxidation and protein and the state of blood antioxidant system 3 and 6 months after the prescription of additional Mildronat and Thiotriazoline in diabetic polyneuropathy patients (M ± m)**

Indexes	The Control	Before treatment	In 2 weeks	In 3 months	In 6 months
The activity of ceruloplasmin (mg / l)	167 ± 8,2	316 ± 8,5 (p<0,01)	185 ± 8,7 (p<0,01)	192 ± 6,2 (p<0,01)	295 ± 8,9 (p>0,05)
The content of reduced glutathione (Mmol / mL)	2,02 ± 0,08	0,86 ± 0,06 (p<0,01)	1,80 ± 0,06 (p<0,01)	1,65 ± 0,05 (p<0,01)	1,12 ± 0,07 (p<0,05)
The content of HS-groups (mmol / 1 ml cr. weight)	2,59 ± 0,08	1,61 ± 0,05 (p<0,01)	2,49 ± 0,09 (p<0,01)	2,37 ± 0,06 (p<0,01)	1,88 ± 0,08 (p<0,05)
The content of malonic aldehyde (mmol / L)	20,4 ± 0,43	33,1 ± 0,51 (p<0,01)	23,2 ± 1,5 (p<0,01)	24,8 ± 1,3 (p<0,01)	27,9 ± 1,7 (p<0,05)
The activity of catalase (mkkat / g protein)	5,3 ± 0,3	3,6 ± 0,2 (p<0,01)	4,8 ± 0,3 (p<0,01)	4,6 ± 0,4 (p<0,05)	3,9 ± 0,5 (p>0,05)
The activity of G-6-FDG (Mmol / min (g Hb)	4,21 ± 0,11	2,76 ± 0,23 (p<0,01)	4,09 ± 0,22 (p<0,01)	3,78 ± 0,18 (p<0,01)	3,25 ± 0,28 (p>0,05)

ketones and aldehydes neutral character ( $\lambda$ 370) (mmol / g protein)	1,51 $\pm$ 0,12	3,26 $\pm$ 0,12 (p<0,01)	1,77 $\pm$ 0,16 (p<0,01)	1,82 $\pm$ 0,18 (p<0,01)	2,94 $\pm$ 0,9 (p>0,05)
ketones and aldehydes of main character ( $\lambda$ 430), (o. O. H / g protein)	19,48 $\pm$ 2,6	41,88 $\pm$ 2,8 (p<0,01)	23,54 $\pm$ 2,5 (p<0,01)	25,68 $\pm$ 1,9 (p<0,01)	34,89 $\pm$ 2,5 (p>0,05)

Note: p - the probability is compared with patients before treatment;

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## NEUROLOGICAL DISORDERS IN PATIENTS WITH ENDOCRINE PATHOLOGY

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#### ABSTRACT

The authors carried out a comparative description of cognitive and emotional personality characteristics of patients with endocrine pathology. It was established that neurosis-like syndrome in patients with primary hypothyroidism was practically obligatory. Patients in most cases complained of mild irritability, tearfulness, emotional lability. Most patients with primary hypothyroidism, regardless of its cause and severity, had a high personal anxiety, and the reactive one was moderate. One of the features of neurosis-like syndrome in primary hypothyroidism is the prevalence of its manifestations in patients with autoimmune thyroiditis and in patients with subclinical hypothyroidism.

**Keywords:** autoimmune thyroiditis, subclinical hypothyroidism, neurosis-like syndrome

**Introduction.** Across the globe, the attention of scientists and clinicians to the problems of etiopathogenesis of neurological disorders in endocrine diseases is increasing. The role of thyroid hormones deficiency in the development of neurological pathology is well-known. Neurological disorders make up a clinical picture for virtually all thyroid diseases, and in some cases they form a syndromic nucleus, being significantly ahead of other manifestations of the disease. However, the issues of the connection between the two systems in the clinical picture is not paid enough attention.

The development of cretinism in children, which manifests itself as a delay in psychoneurological and physical growth is the most severe complication of hypothyroidism. Psychoneurological disorders in children suffering from congenital hypothyroidism are far from having a constant tendency to reverse development, even with the early administration of the substitution therapy. This is due to the significant influence of thy-

roid hormones during the period of the prenatal development of the nervous system and to the inability to eliminate the defect in newborn infants.

Chronic hypothyroid encephalopathy is most often manifested by emotional disturbances. The brain is very sensitive to a deficiency of thyroid hormones in the body. It manifests itself in a depressed mood, a feeling of sorrow and severe depression. Joffe R.T. and Levitt A.J. examined 139 patients with unipolar depression. 19 of them were diagnosed with subclinical hypothyroidism. The authors came to the conclusion that depression in subclinical hypothyroidism differs from that without subclinical hypothyroidism with the presence of panic and ineffective administration of antidepressants. The study by Howland R.H. confirms a connection between hypothyroidism and treatment-resistant depression. 52% of patients with treatment-resistant depression were diagnosed with subclinical hypothyroidism.

The subclinical hypothyroidism patients' cognitive function, memory and attention are impaired as well as their intelligence declines manifestly or masked. Monzani F. et al. in their work evaluated neuropsychological and behavioral features in patients with subclinical hypothyroidism and in the control group. When evaluating them by using the Wechsler Memory Scale, the authors found that the memory in patients with subclinical hypothyroidism was impaired. Determining the Crown-Crisp Experiential Index showed a discrepancy in hysteria, anxiety, somatic disturbances and depression scales between patients with subclinical hypothyroidism and those in the control group. But in general, Crown-Crisp Experiential Index was higher in patients with subclinical hypothyroidism. When the substitution therapy with thyroxine was administered for the patients with subclinical hypothyroidism their memory and cognitive function got improved and their anxiety disappeared. Baldini I.M. et al found the worsening of logical thinking in patients with subclinical hypothyroidism (compared with those suffering from euthyroid goiter) but did not find any affective disorders in them. According to some authors, subclinical hypothyroidism is not the cause of depressive states.

Asthenia, neurosis-like states, insomnia are frequent companions of hypothyroidism as well. So-called "sleep apnea", associated with soft tissue edema of the neck and vocal cords is common, manifesting itself by numerous episodes of respiratory arrest for more than 10 seconds, which is often accompanied by snoring.

Cases of acute psychosis in patients with hypothyroidism of the thyroid gland are also described. In general, the behavior of patients with hypothyroidism is monotonous, equal, a spontaneous, but both exogenous organic psychoses and those approaching, by their structure, the endogenous ones - schizophrenic, manic-depressive and others - can sometimes appear as secondary ones. Anxiety-depressive, delirious and hallucinatory as well as paranoid states are described.

Vestibular atactic syndrome is the best studied among organic disorders. The incidence of this pathology, according to various literature data varies from 10% to 33%. The onset of these disorders is associated with a decrease in cardiac output, a decrease in cerebral blood flow, as well as the use of oxygen and glucose by the neurons of the cerebellum. Adams R. and al explain the development of ataxia by slowing muscle relaxation, rather than cerebellar dysfunction.

In the literature there are also data on extrapyramidal syndrome in case of hypothyroidism.

**The aim of the study.** To improve the effectiveness of medical care for patients with neurological disorders in those with endocrine pathology by studying pathogenetic mechanisms and clinical features in patients with thyroid gland dysfunction, taking into account non-psychotic mental disorders.

**Objectives of the study.** To study neurological disorders in patients with endocrine pathology. To investigate cognitive functions and emotional and personality features of patients with endocrine pathology.

**Materials and methods.** Patients with neurological disorders secondary to endocrine pathology. **Methods:** clinical-neurological and psychodiagnostic ones.

In order to determine the peculiarities of cognitive functions, we used the MMSE test (Mini Mental State Examination), methods of evaluation of attention on the Schultz tables modified by Horbova F.D. and memory was tested by "Memorizing 10 words" (by Luria A.R.). To assess the personal and reactive anxiety, the Spielberg State-Trait Anxiety Inventory scale, adapted by Hanin Yu.L., and the degree of depressive disorders was determined by the Beck A.T. scale.

**Research results discussion.** The study involved 26 patients with hypothyroidism as a result of AIT (autoimmune thyroiditis) and 20 patients with hypothyroidism without AIT. The control group consisted of 20 practically healthy individuals. 34 (73.9%) of patients were on synthetic derivatives of L-thyroxin substitution therapy, and 12 (26.1%) patients had subclinical hypothyroidism. Cognitive impairment was noted in 74.8% of the patients. No one of these patients had severe cognitive impairments leading to a violation of social adaptation. In most patients (64.9%) cognitive impairments were mild. Patients complained of a slight decrease in memory, absent-mindedness, which did not reduce their working capacity and did not lead to a social maladaptation. Among patients with hypothyroidism secondary to AIT and with hypothyroidism without AIT, the incidence of cognitive impairments was practically the same. For instance, in patients with AIT, impaired attention and memory were noted in 75.7% of cases, and in patients with hypothyroidism without AIT in 72.4% of individuals. There were no significant differences in the severity of cognitive impairment in patients of both groups either. Among patients with subclinical and clinical hypothyroidism, there were no significant differences in the incidence or the severity of cognitive impairment. Disturbances in memory and attention were noted in 75.9% of patients with subclinical hypothyroidism. Among patients with clinical hypothyroidism, these disorders were found in 75%.

Neurosis-like syndrome was observed in 93% of the patients under study. Patients complained of slight irritation and emotional lability. In patients with hypothyroidism secondary to AIT neurosis-like syndrome occurred in 91% of cases, in patients with hypothyroidism without AIT - in 97%. The same number of patients with subclinical and those with clinical hypothyroidism complained of high irritability and tearfulness, but it was the patients with subclinical hypothyroidism whose neurosis-like syndrome was more pronounced. The incidence in them was 90%, and in those with clinical hypothyroidism - 94%.

The level of personal anxiety that characterizes it as a character trait on the Spielberg and Hanin scale of anxiety self-esteem had no probable differences in the studied groups and was high in patients both with and without AIT, as well as in patients with varying degrees of severity of hypothyroidism. The average index of personal anxiety in patients with hypothyroidism of the thyroid gland secondary to AIT was  $55.13 \pm 9.62$  points, and in patients with hypothyroidism without AIT -  $53.09 \pm 8.24$  points. In subclinical hypothyroidism, it was  $54.90 \pm 9.10$  points, and in clinical hypothyroidism -  $55.30 \pm 9.02$  points.

The reactive anxiety allows evaluating anxiety as a transient clinical condition. It was moderate in most patients with primary hypothyroidism, regardless of its cause and severity. However, the average index of reactive anxiety was higher in patients with AIT and amounted to  $45.13 \pm 9.20$  points, and in patients with hypothyroidism without AIT -  $32.72 \pm 9.20$  points. The reactive anxiety was also more pronounced in patients with subclinical hypothyroidism and amounted to  $45.95 \pm 8.10$  points, and in patients with clinical hypothyroidism -  $33.80 \pm 8.20$  points.

#### Conclusions.

Neurosis-like syndrome in patients with primary hypothyroidism was practically obligatory. Patients in most cases complained of mild irritability, tearfulness, emotional lability. In the majority of patients with primary hypothyroidism, regardless of its cause and severity, there was a high personal anxiety, and the reactive one was moderate. One of the features of neurosis-like syndrome in primary hypothyroidism is the prevalence of its manifestations in patients with autoimmune thyroiditis and in patients with subclinical hypothyroidism.

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## АКТИВНЫЕ МЕТОДЫ ОБУЧЕНИЯ СТУДЕНТОВ

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## ACTIVE METHODS OF TEACHING STUDENTS

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#### АННОТАЦИЯ

Активные методы обучения способ активного взаимодействия студентов с проблемно-представленным содержанием обучения, в ходе которого он приобщается к объективным противоречиям научного знания и способам их решения, учится мыслить, творчески усваивать знания.

#### ABSTRACT

Active methods of teaching the way of active interaction of students with the problem-presented content of training, in the course of which he becomes attached to the objective contradictions of scientific knowledge and the methods of solving them, learns to think, creatively absorb knowledge.

**Ключевые слова:** активные методы, ролевые игры, компетентностный подход.

**Keywords:** active methods, role play, competence approach.

Активные методы обучения - это система методов, которые обеспечивают активность и многообразие мыслительной и практической деятельности студентов при освоении учебного материала. Студенты обязаны получать глубокие теоретические знания по медицинским дисциплинам, а также овладеть профессиональными мануальными умениями и навыками. Педагогическая технология это модель совместной педагогической деятельности по проектированию, организации и проведению учебного процесса с безусловным обеспечением комфортных условий для преподавателя и студента

[1,2]. Совершенствование профессиональной подготовки кадров на основе компетентностного подхода определяют необходимость разработки и применения инновационных образовательных технологий. Внедрение активных инновационных методов обучения на стоматологическом факультете приводит к тому, что обучающийся становится активным участником образовательного процесса. Это позволяет формировать активную личность, обладающую всеми нужными навыками и качествами современного квалифицированного специалиста. Обучаемый усваивает информацию быстрее,

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