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PATHOGENETIC TREATMENT OF DIABETIC POLYNEUROPATHY

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.*

Key words: *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 (λ 370) and main character (λ 430). 6 months after treatment, these figures hardly differed from the corresponding parameters the patients had shown before taking treatment.

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

Note: p - the probability is compared with patients before 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 (λ 370) and the main character (λ 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 (λ 370) by 66.1% and ketones and aldehydes of the main character (λ 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.

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