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THE EFFECTIVENESS OF MILGAMMA–N THERAPY IN PATIENTS WITH PERIPHERAL DIABETIC NEUROPATHY

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Abstract. Peripheral diabetic neuropathy (PDN) is a severe complication that develops in diabetic patients. Several clinical trials measured the effectiveness of different therapeutical regims for PDN, from which the use of Milgamma-N (Benfotiamine) preparations represents a recent promising option. The paper presents our experience in treating patients with Milgamma-N preparations and assessing the effectiveness of the treatment using a standard paraclinical assessment protocol.
Keywords: diabetes, peripheral neuropathy, Benfotiamine, paraclinical assessment

Rezumat. Neuropatia periferică diabetică este o complicație severă ce apare la pacientul diabetic. Cercetări clinice numeroase au evaluat eficiența diferitelor terapii între care şi folosirea Milgamma-N (Benfotiamina), preparat care pare foarte promițător. Lucrarea prezintă rezultatele unui studiu experimental (cu autocontrol) care evaluează cu ajutorul unui protocol paraclinic de examinare eficiența unui tratament cu Milgamma-N în neuropatia periferică a pacientului diabetic.
Cuvinte cheie: diabet, neuropatie periferică, Benfotiamină, evaluare paraclinică

INTRODUCTION

The peripheral vascular and nervous complications which occur during the course of diabetes mellitus (DM) represent a frequent source of physical and psychological complaints in these patients and, in the same time an important health problem. It is well recognized that some diabetic patients develop a specific painful condition known as diabetic peripheral neuropathy (DPN). Improving these complaints represents a major target for many therapeutic protocols prescribed for the diabetic patients. By this self controlled study, we tried to assess the effectiveness of a treatment with Milgamma-N (Benfotiamine) in diabetic patients with peripheral neuropathy.

MATERIAL AND METHOD

The study covered a period of 4 month, between September and December 2001, and it was aimed to check for the effectiveness of an antidiabetic treatment with Milgamma-N in these patients. The self controlled group consisted of 31 adult patients, aged between 25 and 78 years, with a slightly male predominance.

All patients had diabetes mellitus for more than 5 years and they had already developed symptoms of peripheral diabetic neuropathy (PDN).

Because the age is a significant determinant of clinical symptoms and follow-up of diabetes, three broad ranges of patients'age have been used : group 1 of 9 patients between 24-39 y ; group 2 of 11 patients (40-59 y) and group 3 of 11 patients (over 60 y age).

We presumed that, if the use of Milgamma is efficient in these patients, the results of specific biochemical and electrophysiological tests would outline this progress. Decreased values for blood glucose, cholesterol and triglycerides levels and improved results of standard tests for peripheral vascular and nervous system would be recorded in this case.

A number of paraclinical tests and procedures have been performed in order to assess patients' metabolic and reactive-functional status and correlate the results with the status of their diabetic process:

1. Clinical laboratory tests: blood glucose, total cholesterol and triglycerides;
2. Functional testing (electrophysiological) procedures:

- motor nerve conduction velocity (NCV) studies on the peroneal and sural nerves;
- lower limb (calf) oscillometry for measuring the oscillometric index (O.I.) in the calf;
- electrocardiographic (ECG) and electro-encephalographic (EEG) recordings for assessing the general reactive status.

These tests were performed before and after prescribing the drug regimen consisting of Milgamma-N (a combination of Benfotiamine and a complex of vitamins B). The dosage was 1 cps of Milgamma x 3 times daily (3 x 50 mg = 150 mg Benfotiamine daily) for 2 months.

The statistical analysis was done by means of t-Student test. The level of significance was $p < 0.05$.

RESULTS AND DISCUSSION

Figure 1 and 2 shows the age and sex distribution of diabetic patients.

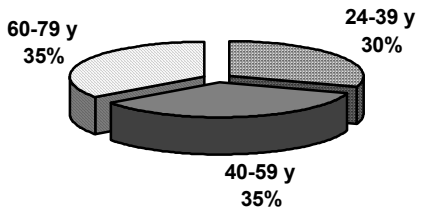

Fig. 1 Age distribution of diabetic patients

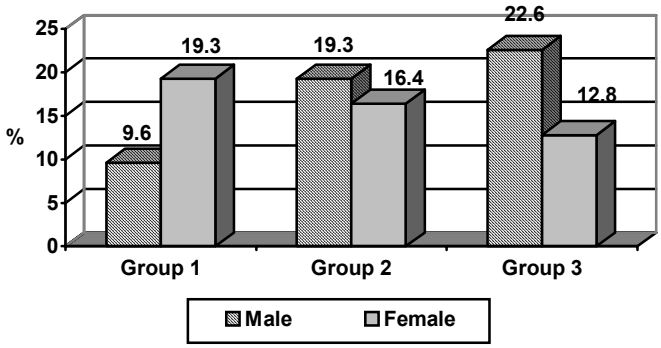

Fig. 2 Sex distribution of diabetic patients

Tables 1 and 2 summarized performed tests values before and after Milgamma-N administration (mean value ± SD). After 60 days treatment with Milgamma-N these values decreased as indicate table 1 data.

Glucose and triglyceride levels dropped significantly after Milgamma administration (except the elderly patients of group 3) as well as the cholesterol concentrations.

Table 1. Laboratory tests in diabetic patients before and after Milgamma-N administration

Patient group		Laboratory findings ($\bar{x}$ ± SD)		
		Blood glucose (g/L)	Cholesterol (g/L)	Triglycerides (mg/dl)
Group 1	A	2.90 ± 0.52	2.17 ± 0.40	271.11 ± 85.14
	B	1.56 ± 0.38	1.84 ± 0.17	202.22 ± 18.38
	p	< 0.001	< 0.05	< 0.05
Group 2	A	2.86 ± 0.93	2.53 ± 0.41	298.33 ± 79.59
	B	1.84 ± 0.59	2.00 ± 0.15	208.08 ± 40.32
	p	< 0.01	< 0.001	< 0.003
Group 3	A	2.49 ± 1.49	2.53 ± 0.40	275.60 ± 104.23
	B	2.13 ± 1.47	2.06 ± 0.38	212.70 ± 84.59
	p	NS	< 0.05	NS

A – before Milgamma administration B – after Milgamma administration

The normal values for the electro-physiological tests included into the protocol were: 50-55 m/sec for motor NCV and 3 for OI (in the lower third of the calf).

Initially, all patients had lower values of both motor nerve conduction velocity and oscillometry index (table 2).

Table 2. The nerve conduction velocity and oscillometric index values before and after treatment

Patient group		Nerve conduction velocity (m/sec) ($\bar{X} \pm SD$)				Oscillometry index (OI) ($\bar{X} \pm SD$)	
		Sural nerve		Peroneal nerve			
		Right	Left	Right	Left	Right	Left
Group 1	A	38.56±1.33	39.22±2.17	38.67±1.80	39.22±4.15	2.06±0.30	2.00±0.25
	B	43.78±2.17	44.11±2.62	44.00±2.18	44.22±2.77	3.13±0.42	3.11±0.42
	p	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
Group 2	A	37.00±1.41	37.25±2.34	38.00±3.41	37.00±3.02	2.52±1.73	2.54±1.72
	B	41.83±2.66	42.25±3.17	42.17±2.37	42.75±3.72	3.37±1.20	3.38±1.21
	p	< 0.001	< 0.001	< 0.003	< 0.001	NS	NS
Group 3	A	36.80±1.93	37.50±2.32	36.90±1.91	37.70±3.40	2.00±0.91	2.80±0.63
	B	39.60±1.26	40.60±2.32	40.00±1.63	41.10±3.03	2.03±1.00	2.85±0.67
	p	< 0.003	< 0.01	< 0.001	< 0.05	< 0.05	< 0.05

A – before Milgamma administration B – after Milgamma administration

The motor NCV values improved significantly for all patients after the treatment with Milgamma-N as table 2 data indicate.

The oscillometry index has been significantly higher in younger patients as well as in elderly ($p < 0.001$ and $p < 0.05$, respectively).

The frequencies of patients with normal OI index after the Milgamma treatment decreased as patient age increase: 77.8 in group 1; 66.7 in group 2 and 50.0 in group 3, indicating a higher benefit for younger patients.

The ECG recordings also revealed ventricular depolarization abnormalities in most patients before receiving Milgamma-N, with flat or isoelectric T-waves. The cerebral bioelectric activity (EEGs) was also modified, with low-amplitude alpha rhythms of 25% patients and alpha rhythms of increased

amplitude of the other 75% patients. The analysis of ECG and EEG recordings showed that the bioelectrical activity returned to normal in most of the patients after receiving the treatment.

A certain improvement of the clinical findings appeared during the follow up period. The patients experienced a reduced level of peripheral pain and an increase of their physical and mental performances. These improvements were more obvious in younger patients.

In is generally accepted that deficiencies in B vitamins, especially B6 and B12, contribute to the development of peripheral diabetic neuropathy. Vitamins B1, B2, B6 and B12 supplies may be benefic for some diabetic patients, because of their role in the proper functioning of the nervous system. Because high doses of vitamin B6 (pyridoxine) can cause a form of neuropathy, the daily dose should not exceed 200 mg. The most useful preparations contain B1, B12 and folate. Also, the multivitamins including vitamin E and B complex (the ”stress” complex) are useful in a peripheral neuropathy (1).

Benfotiamine, which is commercially available in different dosages and pharmaceutical combinations as Milgamma, has recently emerged as an efficient treatment for patients with DPN. Several clinical studies focused on defining the optimum dosage of Benfotiamine (2) or on the use of Benfotiamine in different combinations with vitamins B complex (3,4) for inducing a significant improvement of the peripheral pain in diabetic patients. The same studies (2,4) also describe the use of standard investigations protocols for assessing the therapeutical effect of Milgamma treatment.

The clinical assessment of pain is generally performed by using visual analogue scales and the measurement of the vibratory sense threshold by Rydel-Seiffer biothesiometer technique (4). The evaluation of the peripheral neuropathy is performed by NCV studies or evoked sympathetic potential recordings, sometimes associated with specific cardiovascular tests (2,3).

In our study, we used a protocol that included basic paraclinical tests and procedures for assessing patients with DPN. The biochemical parameters (blood glucose, total cholesterol and triglycerides) evaluated the metabolic conditions of the diabetic patient, while the functional recordings (ECG, EEG, NCV studies and oscillometry) offered the picture of the central and peripheral nervous status and reactivity.

Based on our results, we consider that Milgamma in combination with vitamins B complex is able to improve the local (peripheral) condition of the diabetic patient. As a consequence, the activity of ionic pumps in cardiac and nervous cells was improved, and the ECG and EEG recordings reflected these favorable changes. The NCV studies were able to show both the early occurrence of the peripheral neuropathic process and its course during different

diabetic stages. We, as other authors also do, consider this protocol as very useful for monitoring the course of the diabetic process and for preventing the occurrence of severe complications, such as the diabetic foot or peripheral skin ulcers. In a study at the University of Athens (5), it was shown that regular, long-term use of vitamins B1, B12 and B6 in diabetics was very effective both for improvement in nerve conduction and relief of pain. Improvement of nerve conduction velocity occurred after 4-8 weeks of therapy; these results being similar to those of our study.

CONCLUSIONS

Our results support the idea that Milgamma-N is able to influence in a favorable manner the diabetic peripheral neuropathy (DPN). The consequence of this fact is a real improvement of the peripheral vascular and nervous condition of diabetic patients, especially in younger ones; so, Milgamma-N should be used early as soon as the diagnosis is certain.

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