Type of Diabetes Mellitus Has Influence on Electrophysiological Parameters

Enra Suljic¹, Senad Drnda²

¹Department for Science, Teaching and Clinical Trials, Clinical Centre University of Sarajevo, Sarajevo, Bosnia and Herzegovina
²Department for Urgent Neurology, Clinic for Neurology, Clinical Centre University of Sarajevo, Sarajevo, Bosnia and Herzegovina

ORIGINAL PAPER

ABSTRACT

Introduction: Compulsory electromyoneurography (EMNG) analysis of all neurophysiological parameters, including the most sensitive parameter for early detection of diabetic polyneuropathy (cutaneous silent periods), in patients without subjective symptoms, and EMNG analysis demonstrates the existence of incipient signs for polynomial neuropathy due to which timely therapeutic approach is needed to prevent complications of diabetic disease and prevent irreversible changes in peripheral nerves. Aim: Examine the influence of type diabetes mellitus, therapeutic modality, and gender of patients on neurophysiological parameters obtained by EMNG analysis. Methods: The study included 90 patients with diabetes who were divided into three groups of 30, depending on the duration of the disease. Group 1 consisted of 30 respondents with type 2 diabetes mellitus and up to 5 years of disease duration. Group 2 consisted of 30 respondents with type 2 diabetes mellitus type 5 to 10 years of disease duration. Group 3 consisted of 30 respondents with Type 1 diabetes mellitus. An electron-neurography analysis of peripheral nerve in the extremities was performed. Results: Group 1 (50%) and group 2 (56.17%) respondents had statistically higher incidence of tingling than those in Group 3 (13.3%), p=0.004. Tingling was not statistically significantly different in relation to the examined groups (p=0.314). Reflexes were statistically the most preserved in Group 3 (86.7%), p = 0.001. Measurement of motor conductivity values at median nerve had a significant difference in all parameters (distal latency, amplitude, mean conduction velocity (MCV) and latency in the group with DM type 1, compared to respondents with DM type 2. The same significant difference between all parameters was found when testing peroneus nerve. When measuring motor velocity conductivity in ulnar nerve, there was no significant difference in amplitude, while DM1 type 1 patients had significant differences in values: distal latency and MCV p<0.0001, latency p<0.002. Measurement of sensory velocity was not statistically significant between patients with DM types 1 and 2. In relation to therapy, oral insulin therapy was not shown to be of statistical significance, except for tibialis amplitude measurements, where insulin-treated DM patients had a value amplitude of 12.96±1.48, and in oral therapy group less than 0.04 (p<0.05) 9.14±0.93. In the DM type 2 group no, neurophysiological parameters showed significant gender differences, while in respondents with DM type 2, where the disease lasted shorter, a significant gender difference was present in terms of motor velocity and sensory conductivity in all the nerves examined, except MCV in ulnar nerve. In the DM type 1 respondents, a significant gender difference was present in measuring MCV at tibial nerve and peroneus nerve (p <0.01 and p <0.02), as well as latency of MCV in H reflexes (p<0.01), in males was 56.25±1.03 and in females 32.89±0.47. Conclusion: Diabetic polyneuropathy is significantly more present in patients older than 60 years who have type 2 diabetes mellitus (2/3 of those with a duration of 5 years or less and in ½ respondents with DM duration of less than 5 years), without any hesitation on the type of therapy. Measurement values of motor conductivity at median nerve had a significant difference in all parameters (distal latency, amplitude, MCV, and latency F) in the group with DM type 1. The same significant difference between all parameters was also found in n. peroneus. Distal latency values at sural nerve and tibial nerve, latency values and MCV in H reflexes, do not depend on DM type.

Key words: diabetes mellitus, polyneuropathy, neurophysiology, EMNG.

1. INTRODUCTION

Diabetes is the most common cause of all neuropathy cases, 66% of patients with diabetes mellitus (DM) type 1 and 59% with DM type 2 will develop symptomatic polyneuropathy during life (1-4). It usually has insidious onset and slow devel-
opment, most commonly as distal axonopathy and includes distal slow progression along nervous fiber associated with sensory and motor function disorders (5, 6). The prognosis of untreated diabetic polyneuropathy of the sensory-motor type is poor and the clinical course fluctuates from a significant loss of sensitivity and motor weakness to extremity amputation, which again leads to a lower quality of life (7-9). Neurophysiological tests provide a precise assessment of peripheral nerve function and are actually the only objective indicator and evidence of nerve damage. Mandatory electromyurosurgery (EMNG) analysis of all neurophysiological parameters, including the expected most sensitive parameter for early detection of diabetic polyneuropathy (cutaneous period of silence), in patients without subjective symptoms, and by EMNG analysis we demonstrate the existence of incipient signs for polyneuropathy, which can be prevented by timely therapeutic approach to complications of diabetic disease and prevent irreversible changes in peripheral nerves (10-13). Clinical classification of diabetic neuropathy is divided into diabetic polyneuropathy, focal and multifocal neuropathy (proximal diabetic neuropathy, compressive neuropathy, neurological neuropathy and truncal radicular neuropathy) and autonomic neuropathy. Among the above-mentioned forms, most common is distal polyneuropathy (72% of patients), carpal canal syndrome (12%), other mononeuropathy (6%), and other neuropathies (10%) (Figure 1). It should be borne in mind that approximately 10% of people with diabetes mellitus have some other forms of neuropathy (not induced by diabetes) (14, 15).

2. AIM

Examine the influence of diabetes mellitus type, therapeutic modality, and sex of patients on neurophysiological parameters obtained by EMNG analysis.

3. METHODS

The study included 90 patients with diabetes divided into three groups of 30, depending on the duration of the disease, and a control group of 60 non-diabetic respondents or other polyneuropathy patients. Group 1 consisted of 30 respondents with type 2 diabetes mellitus and up to 5 years of disease duration. Group 2 consisted of 30 respondents with type 2 diabetes mellitus and with disease duration from 5 to 10 years. Group 3 consisted of 30 patients with Type 1 diabetes mellitus. The experimental groups included patients who were referred to the EMNG analysis at the EMG cabinet of the Neurology Clinic, Clinical Center of Sarajevo University and the Neurophysiological Laboratory in Ljubljana in the period from July 1, 2011 until May 1, 2016. The study is prospective, experimental-laboratory, clinically applicable. Before entering the study, respondents had to meet inclusion criteria, and patients who had the exclusion criteria were not evaluated. Both sexes with diabetes mellitus who were referred to EMNG analysis by physicians and respondents who were able to provide adequate responses in data collection patterns were included in the study. Exclusion criteria were: patients who provided incomplete data, deterioration of the underlying disease or general condition of the patient, exclusion request, psychotic patients, patients with metabolic disorders who are on hemodialysis, who suffer from other illnesses that may have the effect on polyneuropathies such as chronic alcoholism, amyloidosis, collagen vascular disease, sarcoidosis, polyradiculoneuritis, malignant diseases and those who have been subjected to neurotoxic agents etc.

Electroneurographic analysis of extremities peripheral nerves:

- Analysis of median nerve (n. medianus) and ulnar nerve (n. ulnaris) at the upper right limb:
  - Terminal motor latency for median and ulnar nerve,
  - Amplitude wave M for median and ulnar nerve,
  - Motor conduction velocity for median and ulnar nerve,
  - F wave latency for median and ulnar nerve.

- Analysis of peroneus (n. peroneus) and tibial nerve (n. tibialis) on the right lower limb:
  - Distal motor latency for peroneus and tibial nerve,
  - Amplitude of wave M for peroneus and tibial nerve,
  - Motor conduction velocity for peroneus and tibial nerve,
  - F wave latency for peroneus and tibial nerve,
  - Hoffmann (H) reflexes by tibial nerve stimulation.

- Measurement of “cutaneous period of silence” by stimulation of tibial nerve.

Sensory neurography of the right hand and right leg:

- Amplitude of neurograms for median and ulnar nerves,
- Sensory conduction velocity (SCV) for median and ulnar nerves,
- Sensory conduction velocity (SCV) for peroneus and tibial nerves.

The above-mentioned neurophysiological parameters were also measured in healthy controls. If the distribution of continuous variables is symmetric, the results are presented as the mean ± standard error of mean value, and for comparison of these variables, the parametric tests (Student’s t-test) were used. If the distribution of continuous variables is not symmetric, median and interquartile ranges were used for the mean value and dispersion measurements and for comparison non-parametric tests. Pearson’s and Spearman’s rank correlation coefficients were used to investigate the linear relationship between the ratio and the ordinal characteristics. The threshold of statistical significance is the conventional level of p=0.05. The study was conducted in accordance with the principles of the current Helsinki Declaration and all local and global ethical standards, and after obtaining the consent of the competent Ethics Committee of the University Clinical Center Sarajevo.

4. RESULTS

In group 1 (63.3%) and group 2 (60%) male respondents were more present. Group 3 (69%) and control group (61.7%) were dominated by female respondents. Using ANOVA analysis, a statistically significant difference in the mean age of the respondents in the group 3 and the average age of the examinees of the other examined groups was established, F=107.49; p=0.001. The average age of group 3 respondents was 19.83±3.58 years. In group 1, the average age of the respondents was 56.3±14.16
Type of Diabetes Mellitus Has Influence on Electrophysiological Parameters

Table 1. Frequency of clinical parameters of respondents with diabetes mellitus (numerical and percentage of clinical parameters is presented in Table 1. Frequency of clinical parameters of respondents with diabetes mellitus)

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Numbness</th>
<th>Tingling</th>
<th>Reflexes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Br. %</td>
<td>Br. %</td>
<td>Br. %</td>
</tr>
<tr>
<td>Group 1</td>
<td>15</td>
<td>60.0</td>
<td>5</td>
</tr>
<tr>
<td>Group 2</td>
<td>17</td>
<td>56.7</td>
<td>9</td>
</tr>
<tr>
<td>Group 3</td>
<td>4</td>
<td>13.3</td>
<td>2</td>
</tr>
<tr>
<td>Total</td>
<td>36</td>
<td>40.0</td>
<td>16</td>
</tr>
</tbody>
</table>

Table 2. Neurophysiological differences between Type 1 and Type 2 diabetes mellitus patients (neurophysiological parameters as mean ± standard error of mean (X ± SEM))

```plaintext
<table>
<thead>
<tr>
<th>GROUP</th>
<th>Numbness</th>
<th>Tingling</th>
<th>Reflexes</th>
</tr>
</thead>
<tbody>
<tr>
<td>MEDIAN N. MOTOR</td>
<td>DM type 1</td>
<td>DM type 2</td>
<td>p</td>
</tr>
<tr>
<td>Latency</td>
<td>4.47±0.13</td>
<td>3.59±0.10</td>
<td>0.001</td>
</tr>
<tr>
<td>Amplitude</td>
<td>8.28±0.83</td>
<td>12.41±0.52</td>
<td>0.001</td>
</tr>
<tr>
<td>MCV</td>
<td>51.19±0.59</td>
<td>57.75±1.04</td>
<td>0.001</td>
</tr>
</tbody>
</table>

MEDIAN N. SENSORY
| Latency     | 3.45±0.09 | 3.16±0.10 | NS |
| Amplitude   | 16.20±1.62 | 22.40±2.08 | 0.02 |
| SCV         | 41.12±1.10 | 45.73±1.24 | 0.01 |

ULNAR N. MOTOR
| Latency     | 29.47±0.41 | 27.19±1.06 | 0.0001 |
| Amplitude   | 9.68±0.68 | 9.46±0.32 | NS |
| MCV         | 53.50±0.69 | 58.71±2.1 | 0.0001 |

ULNAR N. SENSORY
| Latency     | 3.17±0.10 | 3.11±0.09 | NS |
| Amplitude   | 15.80±1.28 | 19.40±1.94 | 0.01 |
| SCV         | 45.3±1.13 | 45.50±1.17 | NS |

PERONEUS
| Latency     | 5.24±0.22 | 4.35±0.23 | 0.001 |
| Amplitude   | 4.03±0.36 | 5.87±0.48 | 0.0002 |
| MCV         | 39.38±1.35 | 43.62±1.68 | 0.0001 |

TIBIAL N.
| Latency     | 54.52±3.04 | 48.66±3.81 | 0.01 |
| Amplitude   | 9.45±0.23 | 9.49±0.25 | NS |
| MCV         | 37.05±1.11 | 43.47±0.99 | 0.0001 |

SURAL N.
| Latency     | 54.48±2.54 | 49.1±2.32 | 0.02 |
| Amplitude   | 4.41±0.34 | 4.13±0.29 | NS |
| SCV         | 29.87±2.00 | 31.40±1.89 | NS |

H REFLEX
| Latency     | 36.08±2.25 | 34.01±0.54 | NS |
```

Table 3. Neurophysiological differences between patients with diabetes mellitus treated with per os and insulin therapy (neurophysiological parameters as mean ± standard error of mean (X ± SEM))

2. The same significant difference between all parameters was found in the test of peroneus nerve. When measuring motor velocity conductivity of ulnar nerve, there was no significant difference in amplitude, while DM type 1 patients had significant differences in values: distal latency and MCV p<0.0001, latency F<0.002. Measurements of motor conduction velocity did not show statistically significant differences between patients with DM type 1 and 2.

Distal latency values at sural and tibial nerve were not significantly different in relation to type DM, while amplitude values were shown to be more significant markers for patients with DM type 1.

The latency values and MCV in H reflexes were not significantly different between DM type 1 and DM type 2 patients. Of the total number of respondents with diabetes mellitus, 28.9% used per os therapy, while 71.1% of respondents were treated with insulin therapy. In group 1, insulin therapy was used by 40% of respondents, and oral therapy was used by 60% of patients. In group 2, 26.7% of respondents used per os therapy, while 73.3% used insulin therapy. All respondents in group 3 used insulin.

Analysis of clinical parameters in Table 1 indicated that respondents in group 1 (50%) and group 2 (56.17%) had statistically higher numbness compared to group 3 (13.3%). p=0.004. Tingling was not statistically significantly different in relation to the examined groups (p=0.314). Reflexes were statistically most preserved in group 3 (86.7%), p=0.001.

Measurement values of motor conductivity at median nerve had a significant difference in all parameters (distal latency, amplitude, motor conduction velocity (MCV) and latency) in the DM type 1 group compared to respondents with DM type 2. The same significant difference between all parameters was found in the test of peroneus nerve. When measuring motor velocity conductivity of ulnar nerve, there was no significant difference in amplitude, while DM type 1 patients had significant differences in values: distal latency and MCV p<0.0001, latency F<0.002. Measurements of motor conduction velocity did not show statistically significant differences between patients with DM type 1 and 2.

Distal latency values at sural and tibial nerve were not significantly different in relation to type DM, while amplitude values were shown to be more significant markers for patients with DM type 1.
cantly lower (p<0.05) 9.14±0.93.

Table 4 shows neurophysiological differences in relation to gender in groups of patients with diabetes mellitus (Neurophysiological parameters as mean ± standard error of mean (X ± SEM)).

5. DISCUSSION

The most common complications of the nervous system in diabetes mellitus are peripheral, symmetrical lower extremity neuropathy, with motor and sensory function deterioration (16). Diabetic polyneuropathy is one of the major complications of diabetes mellitus. It belongs to the group of mixed axonal demyelinating sensory-motor polyneuropathies and in the group of vascular neuropathies, and is considered to be caused by changes in the peripheral nerves blood vessels (17, 18). The pathogenesis of peripheral nerve disorders in diabetes is not yet definitively clarified and there are a several theses: ischemia due to atherosclerotic changes or diabetic microangiopathy, then accumulation of lipids in Schwann cells that later disturb the normal activity and function of these cells, then the thesis about the enzyme disorder, some kind of osmotic damage or disturbance in transport or that it is even about trauma and some immune disorders. Clinical signs depend on the degree of damage and the type of damaged nerve fibers, within the peripheral nerve. Consequently, the clinical picture may be dominated by predominantly sensory or motor symptoms with signs of damage of also the autonomous nerve fibers. Basic pathological changes are primary axonal degeneration and secondary segmental demyelization (18). EMG is a key diagnostic procedure in patients suspected of neuropathy because it can primarily confirm neuropathy, to distinguish axon and demyelinating, to locate neuronal lesions (proximal, distal, motor, sensory fibers) to register denervation potential (fibrillation, fascicula-
tions and positional maintenance potentials) to diagnose the degree of muscular damage. EMNG analysis in clinically evident polyneuropathy verifies decrease of both sensory and motor velocities, particularly at the lower extremities where peripheral nerves are the longest and often the rate of deceleration of the rate of impulse delivery is proportional to the severity of the underlying disease (18). EMNG is most commonly used to diagnose peripheral nervous system disorders. Peripheral nerve lesions can primarily result in loss of axon or myelin (demyelination), resulting in different EMNG finding patterns (2, 6, 9). Demyelization is associated with significant decrease in impulse delivery velocity (slower than 75% of the lower limit of normal values), significant prolongation of distal latencies (exceeding 130% of the upper limit of normal values), or both. In 1961 Lawrence and Locke (19) in their study of patients with diabetic neuropathy confirmed a statistically significant difference in the conductivity velocity of motor fibers in median nerve (10 m s) and peroneus nerve (11 m/s) compared to the healthy control group. Gilliat and Willison in 1962 (20, 21) confirm the existence of a significant decrease in the conductivity velocity of the examined nerve, and similar results were obtained by Thomas and Lascelas in 1966 (22) and Chopra in 1969 (23). Berger (24) obtained the results of a drop in conductivity velocity in motor nerves, caused by the process of primary demyelination or motor conduction block. Dyck in 1985 (25) states the slowing in velocity of transmitting along the motor fibers as the first sign of diabetic neuropathy. Millán-Guerrero et al. (26) conducted a study aimed at detecting diabetic polyneuropathy among adult patients and clinical evaluation by Hoffmann reflex. In addition, the predictive value of H-reflex in the diagnosis of diabetic polyneuropathy was also evaluated. The study included 150 adult patients, who were referred to neurophysiological examination and electrophysiological testing (H-reflexes and nerve conduction velocity). The results indicate that H-reflex was absent in 39.3% (59/150), and the delay was present in 43.3% (65/150) of patients, which is not correlated with the results of this study. The motor conductivity of ulnar nerve showed a prolonged delay in 9.3% (14/150) patients. The conclusion states that the logistic regression analysis shows that H-reflex is significantly associated with positive results. The analysis of clinical parameters indicated that group 1 (50%) and group 2 (56.17%) had statistically higher incidence than group 3 (13.3%), p=0.004. Tingling was not statistically significantly different in relation to the examined groups (p=0.314). Reflexes were statistically the most preserved in Group 3 (86.7%), p=0.001. Kakrnai et al. (27) conducted a two-goal study, which was aimed to analyze gender and neuropathy in patients with type 2 diabetes mellitus and to associate clinical polisteropathy with nerve conduction studies. The study included 50 respondents, who developed diabetes after 30 years of age. Polynucleotide symptoms have been analyzed. The results indicate that out of the 50 respondents 46 (92%) complained of fever, 32 (64%) stinging on the foot, 29 (58%) had difficulty in moving, 29 (58%) had reduced or lost vibration sensation, and 21 (42%) has a reduced sense of light touch.

6. Conclusion

Diabetic polyneuropathy is significantly more present in patients older than 60 who have type 2 diabetes mellitus (2/3 of respondents with a duration of 5 years or less in ½ respondents with DM less than 5 years of age), without difference according to the type of therapy. Measured values of motor conductivity at median and peroneus nerve had a significant difference in all parameters (distal latency, amplitude, MCV and latency F) in the group with DM type 1. Distal latency values at sural and tibial nerve, latency values and SCV in H reflexes, does not depend on DM type.

Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent forms.

Author’s Contribution: Both authors gave substantial contribution to the conception or design of the work and in the acquisition, analysis and interpretation of data for the work. Each author had role in drafting the work and revising it critically for important intellectual content. Each author gave final approval of the version to be published and they agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

References

Type of Diabetes Mellitus Has Influence on Electrophysiological Parameters


