The Value of Nerve Conduction Study and F-Wave Latency in Subclinical Neuropathic Type II Diabetic Patients

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Abstract
The purpose of this study is to evaluate the clinical usefulness of electrophysiological indexes in detecting and preventing diabetic neuropathy, it is important to identify subclinical diabetic neuropathy with no objective clinical or electrophysiological abnormalities, in which routine nerve conduction study often fails to detect early stage of neuropathy.

Two subject groups were included in this study, patients with DM and control subjects. The routine nerve conductive study (NCS) and F-wave were conducted in 35 patients with type II diabetes mellitus but without symptoms and signs of lesions of nervous system.

Conduction velocity (SCV) and sensory amplitude (Amp) were measured for median, ulnar and sural nerves as well as distal motor latency (DML), motor conduction velocity (MCV), motor amplitude (Amp) and F-wave latency were measured for median, ulnar and tibial nerves in DM patients and their control group.

Our results showed that there were significant differences between the controls and the DM group (p<0.05). The prolonged F-wave latency represent the main abnormalities and the involvement of the sensory fibers are more than that of the motor fibers and the affection of the lower limbs nerve are worse than that of the upper limbs in diabetic patients when compared with the control group. The most commonly involved nerves are the sural and median nerve sensory fibers. So in this study we concluded that F-wave can be used as a sensitive indicator for the early diagnosis of peripheral neuropathy and it can help to detect the subclinical lesions.

الخلاصة
الهدف من هذه الدراسة هو فحص التغيرات الكهروفيزيولوجية وتعريف الظاهرة السريرية لهذه الاعراض في الإكتشاف المبكر لاعتلال الأعصاب جراء داء السكري ومنعه، من المهم اكتشاف اعتلال الأعصاب غير السريري لمرضى السكري بدون أعراض سريرية أو تغيرات كهروفيزيولوجية واضحة عندما يفشل تخطيط العصب الزوجي في اكتشاف المرحلة المبكرة لاعتلال الأعصاب.

شملت الاستنتاجات الكهروفيزيولوجية لتخطيط الأعصاب المحيطية الكهربائي لمعرفة كفاءة الأعصاب الحسية (كل من العصب الصف (الوسطي) والعصب الرضدي والعصب الزيتي) والأعصاب الحركية مع دراسة موجة F- لكل من العصب الناصف (الوسطي) والعصب الرضدي والعصب الزيتي.

كانت هذه الدراسة مُثيرًا لمصابي داء السكري من النوع الثاني تميزوا جميعهم بخلوهم من أعراض وعلامات سريرية لتاثر الجهاز العصبي.

لا يوجد أي تقييم الأعصاب الحسية يظهر تدهورًا ملحوظًا في كفاءتها أكثر من الأعصاب الحركية وأعصاب الأطراف السفلية أكثر من الأطراف العليا، وبعد العصب الوسطي والزيتي أكثر الأعصاب تأثرًا كما ان زيادة طول الموجة F- بعد من أطراف التغيرات الواضحة.

لذا استنتج من هذه الدراسة موجة F- في التخطيط الكهربائي للأعصاب المحيطية تعد مؤشر دقيق للتشخيص المبكر لاعتلال الأعصاب لمصابي داء السكري.
Introduction
Diabetic neuropathy (DN) is a common complication in patients with diabetes mellitus (DM), approximately 45-70 percent of patients with type II diabetes will develop manifestations of peripheral neuropathy. More importantly, several studies document clinical and subclinical signs of diabetic neuropathy even before neurological impairment and symptom development. [1,2] These cases substantiate the importance of early and intensive glycemic control as the most important preventable risk factor in the development of DN. [3] Some patients with DN are asymptomatic but electrophysiological or nerve biopsy can reveal impairment of peripheral nerves [3,4].

DN does not represent one distinct disease but rather an adverse group of conditions that affect the peripheral nervous system, attacking the peripheral and autonomic nerves and causing both focal and systemic disease. [5]

The specific pathogenic disturbances underlying the etiology of neuropathy has not been completely elucidated, although a recognized link exists between persistent hyper-glycemia and neurological dysfunction. [6]

The F-wave is a late muscle response that results from the antidromic activation of one or a small number of motor neurons following electrical stimulation of peripheral nerve [7]. Kimura et al. [8] focused on use of the F-wave because it allows assessment of the proximal nerve segment, which is not accessible by the conventional nerve conduction studies.

They reported that the F ratio, calculated from the latency of proximal and distal segments of peripheral nerves, was smaller in diabetic patients than in control subjects. They suggested that the distal segment is more dominantly damaged in diabetic polyneuropathy [8].

This study examined asymptomatic patients with DM for the changes in NCV and F-wave with an attempt to evaluate the application of electrophysiological tests in the early diagnosis of sub-clinical neuropathy in peripheral neuropathy.

Patients and Methods
Two subject groups were included in this study, patients with DM and control subjects.

The electrophysiological tests were done at the neurophysiological unit of Mirijan Teaching hospital in Babylon City, during the period Nov/2011-March/2012.

A history was taken, and a complete medical examination and detailed neurological examination were carried out for every patient, all of them were free from any neurological problems, also they were free from other diseases that may affect the nerve function, such as renal failure, systemic lupus erythematosus, hepatic failure.

All of the subjects (patients and control) that were included in this study were informed about the aim and technique of the study and their acceptance was taken.

DM Group: The subjects in the DM group included 35 patients (20 men and 15 women) with subclinical type 2 diabetes mellitus, the age of the patients ranged from 35-60 years, they all satisfied the criteria of American Diabetes Association (ADA, 1997).

Control Group: The control group included 30 subjects (20 men and 10 women), they were aged from (35-60) years.

Neurophysiological assessment (NCS and EMG machine):
Nicolet NCS - EMG machine was used. The stimulus intensity can be manually changed. This system include
four channels preamplifiers and adjusted (0-99) mA.

Nerve Conduction Studies:
The distal sensory latency (DSL), sensory conduction velocity (SCV) and sensory amplitude (Amp) were measured for median, ulnar and sural nerves as well as distal motor latency (DML), motor conduction velocity (MCV), motor amplitude (Amp) were measured for median, ulnar and tibial nerves in (DM) patients and the control group.

The F-wave study:
For recording the F-wave parameters, the skin and electrodes preparations and the handling of the subjects were just like that of the NCS and for the same reason.

The only difference from the NCS is that the of the stimulating electrodes was placed proximally, instead of the anode.

Square pulses of 0.1 msec duration, a frequency of 1 stimulus/sec. and negative polarity were used.

The stimulus intensity was increased gradually to the supramaximal level, that is 50% higher than the current producing the maximal direct muscle response. 15 trials were displayed on the storage oscilloscope automatically shifting successive sweeps vertically, a facility that is provided by the Nicolet F-wave program, and the clearly identified F-waves were recorded and automatically analyzed, manual adjustment of the pointers also is quite possible and easy.

The latency of the F-wave is measured from the stimulus artifact to the onset of the first negative or positive deflection from the baseline for the fastest (F min) that contribute to the antidromic activation of the moternerrous [9].

Results
The distal sensory latency (DSL), Sensory conduction velocity (SCV) and sensory amplitude (Amp) were measured for median, ulnar and sural nerves as well as distal motor amplitude (Amp) and minimal F-wave latency were measured for median, ulnar and tibial nerves in diabetic patients and their tables 1, 2, 3 and the sensory parameters of sural nerve in table 4.

Table 1 The mean ± SD of median nerve sensory and motor conduction parameters of diabetic patients and the control group.

<table>
<thead>
<tr>
<th>parameter</th>
<th>control</th>
<th>diabetic patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSL (m.sec) (mean± SD)</strong></td>
<td>2.20 ± 0.34</td>
<td>2.70 ± 0.51*</td>
</tr>
<tr>
<td><strong>Sensory Amp (µvolt) (mean± SD)</strong></td>
<td>32.50 ± 10.22</td>
<td>31.06 ± 8.67</td>
</tr>
<tr>
<td><strong>Sensory CV (m/sec) (mean± SD)</strong></td>
<td>50.55 ± 7.21</td>
<td>46.38 ± 6.84*</td>
</tr>
<tr>
<td><strong>DML (m.sec) (mean± SD)</strong></td>
<td>2.91 ± 0.58</td>
<td>3.22 ± 0.83</td>
</tr>
<tr>
<td><strong>Motor Amp (m.volt) (mean± SD)</strong></td>
<td>12.38 ± 4.08</td>
<td>11.70 ± 4.14</td>
</tr>
<tr>
<td><strong>Motor CV (m/sec) (mean± SD)</strong></td>
<td>64.98 ± 5.75</td>
<td>62.25 ± 6.77</td>
</tr>
<tr>
<td><strong>F-wave (m.sec) (mean± SD)</strong></td>
<td>24.29 ± 2.39</td>
<td>25.46 ± 3.19*</td>
</tr>
</tbody>
</table>

*Significant = p-value < 0.05
DML: Distal motor latency.
Amp: amplitude.
CV: conduction velocity.
DML: Distal motor latency.
**Table 2** The mean ± SD of ulnar nerve sensory and motor conduction parameters of diabetic patients and the control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>control</th>
<th>Diabetic patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSL (m.sec) (mean± SD)</strong></td>
<td>1.66 ± 0.22</td>
<td>1.78 ± 0.31</td>
</tr>
<tr>
<td><strong>Sensory Amp (µvolt) (mean± SD)</strong></td>
<td>31.47 ± 12.49</td>
<td>29.66 ± 10.54</td>
</tr>
<tr>
<td><strong>Sensory CV (m/sec) (mean± SD)</strong></td>
<td>55.14 ± 3.51</td>
<td>54.32 ± 2.95</td>
</tr>
<tr>
<td><strong>DML (m.sec) (mean± SD)</strong></td>
<td>2.10 ± 0.28</td>
<td>2.06 ± 0.17</td>
</tr>
<tr>
<td><strong>Motor Amp (m.volt) (mean± SD)</strong></td>
<td>9.96 ± 1.12</td>
<td>9.87 ± 0.92</td>
</tr>
<tr>
<td><strong>Motor CV (m/sec) (mean± SD)</strong></td>
<td>60.23 ± 6.00</td>
<td>58.40 ± 5.47</td>
</tr>
<tr>
<td><strong>F-wave (m.sec) (mean± SD)</strong></td>
<td>23.45 ± 0.80</td>
<td>26.77 ± 1.74*</td>
</tr>
</tbody>
</table>

*Significant = p-value < 0.05
DSL: Distal sensory latency.
Amp: amplitude.
CV: conduction velocity.
DML: Distal motor latency.

**Table 3** The mean ± SD of tibial nerve motor conduction parameters of diabetic patients and the control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>control</th>
<th>Diabetic patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DML (m.sec) (mean± SD)</strong></td>
<td>3.06 ± 0.26</td>
<td>3.15 ± 0.36</td>
</tr>
<tr>
<td><strong>Motor Amp (m.volt) (mean± SD)</strong></td>
<td>9.02 ± 1.17</td>
<td>9.25 ± 1.75</td>
</tr>
<tr>
<td><strong>Motor CV (m/sec) (mean± SD)</strong></td>
<td>51.78 ± 7.34</td>
<td>44.12 ± 8.32*</td>
</tr>
<tr>
<td><strong>F-wave (m.sec) (mean± SD)</strong></td>
<td>46.12 ± 1.73</td>
<td>49.06 ± 4.88*</td>
</tr>
</tbody>
</table>

*Significant = p-value < 0.05
DML: Distal motor latency.
Amp: amplitude.
CV: conduction velocity.

**Table 4** The mean ± SD of sural nerve conduction parameters of diabetic patients and the control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>control</th>
<th>Diabetic patient</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DSL (m.sec) (mean± SD)</strong></td>
<td>1.76 ± 1.44</td>
<td>2.11 ± 0.49*</td>
</tr>
<tr>
<td><strong>Sensory Amp (µvolt) (mean± SD)</strong></td>
<td>20.85 ± 4.91</td>
<td>19.83 ± 7.8</td>
</tr>
<tr>
<td><strong>Sensory CV (m/sec) (mean± SD)</strong></td>
<td>46.50 ± 3.39</td>
<td>41.39 ± 9.05*</td>
</tr>
</tbody>
</table>

*Significant = p-value < 0.05
DSL: Distal sensory latency.
Amp: amplitude.
CV: conduction velocity.

Most sensory and motor parameters of some peripheral nerves were measured and their results show different significant levels from the
control group, these results are discussed below:

The DSL of the median nerve was prolonged and the SCV was significantly decreased in diabetic patients (<0.05) when compared with the control group as well as the F-wave of the median nerve was significantly prolonged.

There were no significant alteration in parameters of the ulnar nerve in diabetic patients when compared with that of the control group except the F-wave significantly difference in diabetic patients.

The DSL of the sural nerve was prolonged, and the SCV was also decreased (<0.05) diabetic patients when compared with the control group.

The conductive parameters of the tibial nerve (MCV and F-wave) in diabetic patients statistically were significant when compared with the control group.

**Discussion**

As the American Academies of Neurology and Physical Medicine and Rehabilitation and the American Association of Electrodiagnostic Medicing suggested that electrodiagnostic studies are obviously more accurate for researches than symptoms and signs [10], so a careful electrodiagnostic examination was entirely related on in this study.

As insidious onset of type II diabetes, slow progress, when there is numbness, pain, light and sometimes not pay attention, DPN can be disabled later, seriously affect quality of life. In this study, we meet the nerve conduction and f-wave examination, found that DSL of both median and sural nerves were prolonged as well as the SCV were decreased in diabetic patients, tibial nerve MCV were slower in diabetic patients, the affected nerve conduction parameters in our diabetic group were the distal latencies and conduction velocities, whereas the amplitudes of sensory and motor responses were not significantly different from the control. This suggests that the early diabetic effects on the peripheral nerves are mainly demyelinating.

While there was significant prolongation of f-wave latency regarding the nerves of both upper and lower extremities, this information is consistent with the literature result[11,12], The main advantage of F-wave methodology has been in the detection of peripheral neuropathies in which F-wave may show clinically significant and measurable changes even before conventional nerve conduction studies are informative[7]. This is because the slowing of nerves conduction is maximized by F-waves traveling for long distances over the entire length of the nerve. Different patterns of F-wave abnormality have been demonstrated in patients with various peripheral nerve disorders[7], as well as in diabetic neuropathy[14,15]. Although F-response latency was considered a sensitive indicator of peripheral neuropathy[16], amplitude and duration in ulnar nerve F-response were the other sensitive parameters for the detection of mild diabetic neuropathy in type I diabetes[15]. F-wave study added to conventional nerve conduction studies should provide more information that is useful in diagnosing the early stages of diabetic neuropathy.

Another application of F-wave measurement is in the evaluation of proximal nerve lesions[17]. F-wave studies can provide useful information about patients who have lumbers or cervical root compression[18] or the carpal tunnel syndrome[17]. It would be useful to exclude complications like radiculopathy in patients with diabetes. While several useful F-wave
parameters have been reported, the application of F-waves is mainly limited to latency measurement. Kimura et al [7]. Suggested that the latency ratio of the proximal to the distal segment (Fratio) was reduced in diabetic patients. They concluded that motor conduction abnormalities in diabetic polynueuroopathy were diffuse over the entire length of the nerve, but were more intense in the distal than in the proximal segment. From the above results that, nerve conduction velocity check with the F-wave examination provide the basis for a comprehensive and objective diagnosis of DPN in diabetic patients of type II.

DPN the mechanism is currently considered the following mechanisms: vascular dysfunction, metabolic disorders, lack of neurotrophic factors, laminin deficiency, immune, system abnormalities, oxidative stress. [19,20] long-term high blood sugar disorder of the metabolism, direct damage to Schwann cells or myelin, or axonal Lang hocks, so that NCV slowing, latency, amplitude decreased. While long-term high blood sugar and low metabolic disorders can affect the nerves lining the microvascular structure and function, causing the destruction of blood nerve barrier, and then ischemia, hypoxia, leading to changes in nerve fibers, which is the cause of severe abnormal NCV[21].

**Conclusion**

Nerve conduction velocity and F-wave examination supplemented with a good objective, quantitative, non-invasive and proven reliability, and easy to operate, is the first choice for diagnosis of DPN and important screening method.

So in this study we concluded that F-wave can be used a sensitive indicator for the early diagnosis of peripheral neuropathy and it can help to detect the subclinical lesions.

**References**