Evaluation of motor nerve excitability by subtreshold stimuli in diabetic polyneuropathy

Diabetik polinöropatide eşik altı uyarilarla motor sinir eksitabilitesinin değerlendirilmesi

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Abstract

Purpose: The aim of this study is to evaluate motor nerve excitability in diabetic polyneuropathy.

Materials and methods: Forty-five patients were enrolled and divided into 3 groups (Group I; diabetic patients without polyneuropathy, Group II; diabetic patients with polyneuropathy, Group III; healthy controls,). The stimuli were given to tibial nerve for 100μs with 5 mA increments starting from 5 mA up to the maximum of 100mA. The CMAP amplitudes appearing with each current of stimulus were divided into the maximum CMAP amplitude for each patient. This value is considered as the ratio of recruited motor units (RRMU) for that current. The mean value of the RRMU for each stimulus current in groups II and III were compared with the healthy controls.

Results: The statistical analysis revealed no significant difference in diabetic patients in terms of nerve excitability with the subtreshold stimuli. Besides, the current that is needed to achieve the maximum CMAP amplitude did not differ between the groups.

Conclusion: Giving subtreshold stimuli with increasing currents did not give additional information about motor nerve impairment in diabetic patients.

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Key words: Tibial nerve, excitability, subtreshold stimuli, diabetes, polyneuropathy

Özet

Amaç: Bu çalışmanın amacı diabetik polinöropatide motor sinir uyarılabilirliğini incelemektir.

Gereç ve yöntem: Çalışmaya 45 hasta alınarak 3 gruba ayrıldı (Grup I: polinöropatisi olmayan diabetik hastalar, Grup II: polinöropatisi olan diabetik hastalar, Grup III: sağlıklı kontroller). Tibial sinir 100μs süreyle 5mA'den başlayıp 5'er mA'lik artışlarla maksimum 100mA' e kadar uyarıldı. Her bir uyarı şiddetiyle ortaya çıkan bileşik kas aksiyon potansiyel (BKAP) amplitüdü, elde edilen maksimum BKAP amplitüdüne bölünerek her bir uyarı şiddetiyle rekrüte olan motor ünit oranı hesaplandı. Hesaplanan bu değer gruplar arasında karşılaştırıldı.

Bulgular: Polinöropatisi olmayan diabetik hastalarla polinöropatisi olan diabetik hastalar arasında eşikaltı uyaranlarla motor sinir uyarılabilirliği arasında anlamlı bir fark saptanmadı.

Sonuç: Bu bulgularla, eşik altı uyarıların giderek artan serilerde uygulanmasının diabetik hastalardaki motor sinir hasarı ile ilgili ek bir bilgi sağlamadığı sonucuna varıldı.

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Anahtar sözcükler: Tibial sinir, uyarılabilirlik, eşik altı uyarı, diabet, polinöropati

Introduction

Polyneuropathy is one of the most common complications of diabetes mellitus (DM) type II. Different kinds of polyneuropathy can be seen in DM, however small fiber distal sensory-motor polyneuropathy is the most common one. Among the pathological changes, both axonal loss and demyelination of peripheral nerves are present in diabetic polyneuropathy (DP). In electrodiagnostic studies the amplitude of the compound muscle action potential (CMAP) and conduction velocity may be normal in case of partial axonal and myelin degeneration in DP. [1]. Therefore, nerve conduction studies may not be helpful in the diagnostic workup even in case of clinical neuropathy.

The threshold current, which is necessary to generate action potentials in individual

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motor nerve fibers, depends on axon diameter. Therefore, if a motor nerve is stimulated electrically with successively increasing stimulus strengths, an increasing number of motor units will be recruited which lead to an increased compound muscle action potential (CMAP) amplitude [2]. The evaluation of CMAP amplitudes which are formed by lower stimulus intensities before reaching the maximal CMAP amplitude can help in quantifying the electrical excitability of the peripheral nerve [3, 4]. Besides, the studies that quantify the electrical excitability may help us to understand the physiopathology of the disease.

The aim of this study is to test whether there is an abnormality of tibial nerve excitability with sub-threshold stimuli in diabetic polyneuropathy.

Materials and Methods

Thirty-two (14 female, 25 male) patients with diabetes mellitus type II were included and divided into 2 groups. Group I (n=17; 11 female, 6 male) consisted of diabetic patients without DP; and group II (n=15; 3 female, 12 male) consisted of diabetic patients with polyneuropathy. Thirteen (6 female, 7 male) healthy volunteers were included as control (group III).

The diagnosis of polyneuropathy was made according to clinical criteria. Polyneuropathy was clinically defined as: a) failure to elicit the knee and/or ankle reflexes after reinforcement with or without symptoms of neuropathy or gross sensory disturbance in both feet, b) typical loss of sensation to pin prick and deep pain distally, c) loss of proprioception with sensory ataxia and a positive Romberg sign, or d) symptoms of burning sensation in the feet at night and day [5]. In healthy controls the same clinical evaluations are performed and found to be normal. Serum levels of HbA1c were measured for every participant in order to confirm/exclude the diagnosis of diabetes mellitus type II. The values over 6.0 % reliably confirmed and values below 5.2 % excluded the diagnosis [6].

All of the participants gave their informed consent.

Each of the participants' electrodiagnostic tests were performed including at least 3 extremities and at least 1 motor and 1 sensory nerve conduction study in each extremity to confirm the diagnosis of polyneuropathy. Posterior tibial nerves were always studied. Nerve conduction studies are carried out with a Medelec Premiere electromyograph®.

After routine nerve conduction studies, stainless steel surface electrodes with 6 mm diameter were placed on the middle of abductor hallucis longus and its tendon. The stimulator was placed 8 cm proximal to the active surface electrode just behind the medial malleolus on the ankle. After the best stimulation point of the tibial nerve was determined, the surface stimulator was fixed and during the whole study it was being held at the same point which was fixed in the beginning of the study.

The stimuli were applied for 100μs, with 1 minute intervals and with 5 mA increments starting from 5 mA. The CMAP amplitudes were recorded for each stimulus. Also the lowest current, which caused maximum amplitude of CMAP, was determined for every patient. All these procedures were also applied to the control group. The study was performed in both extremities in each patient. In order to rule out the possible effect of axonal loss the ratio of recruited motor units (RRMU) was calculated for each stimulus; the CMAP amplitudes were divided with the maximum CMAP amplitude in every patient (for instance; RRMU for 50mA = CMAP amplitude at 50mA / maximal CMAP amplitude x 100).

The mean values of the RRMU were obtained for each stimulus between 5 mA and 100 mA for each group and compared.

Statistical Analysis

Statistical analysis was carried out with SPSS for Windows (version 14.0). The RRMUs were compared between groups by Kruskal-Wallis test.

Results

The demographic features are presented according to groups in Table-1. Disease duration was higher in group II than group I ($p < 0.05$). Serum Hba1c levels confirmed the diagnosis of diabetes in groups I and II.

Routine electrodiagnostic studies confirmed the diagnosis of polyneuropathy in group II. As expected, maximum CMAP amplitudes and conduction velocities were lower in group

Table 1. The demographic features and routine EMG findings.

	GROUP I	GROUP II	GROUP III	p VALUE
Age	54.17 ± 4.55	55.00 ± 5.59	51.84 ± 7.30	0.120
Disease duration	8.58 ±7.26	11.14 ±5.33	-	**0.016***
Hba1c	7.07 ± 1.48	9.80 ± 1.94	4.01±0.86	**-**
Max. CMAP amplitude	10.06 ± 4.28	6.31 ±5.27	12.50 ± 8.37	**<0.001***
Distal motor latency	4.33 ± 1.33	5.83 ± 1.13	4.51 ± 1.06	**0.006***
Conduction velocity	44.05 ± 3.65	33.95 ± 5.30	45.88 ± 4.02	**0.000***

II than in groups I and III (p<0.001); the distal motor latency was longer in group II than that of groups I and III (p< 0.05).

The mean stimulus current, which is needed to achieve the maximum CMAP amplitude was 67.87 ±20.28 mA for group I; 74.00±14.86 mA for group II and 68.75±19.59 mA for group III (not significant).

Table-2 presents the mean values of RRMU for each stimulus current and the statistical analysis revealed no difference between groups. Figure-1 summarizes these findings.

Table 2. Mean RRMU values and standard deviations

	GROUP I	GROUP II	GROUP III	p VALUE
5 mA	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1,000
10 mA	0.0 ± 0.0	0.0 ± 0.0	0.0 ± 0.0	1,000
15 mA	0.34 ±1.42	0.33 ± 1.84	1.24 ± 4.20	0.451
20 mA	2.32 ±5.47	2.49 ± 7.98	5.94 ± 15.64	0.209
25 mA	11.07 ± 17.82	7.55 ± 14.26	11.47 ± 22.93	0.626
30 mA	21.95 ± 24.47	12.13 ± 19.21	18.80 ± 28.99	0.203
35 mA	33.75 ± 31.10	20.27 ± 23.72	28.59 ± 35.08	0.153
40 mA	46.07 ± 36.93	30.09 ± 29.54	38.40 ± 38.88	0.176
45 mA	56.22 ± 36.56	39.00 ± 35.20	48.84 ± 37.97	0.117
50 mA	62.27 ± 35.16	47.80 ± 36.92	57.19 ± 37.68	0.162
55 mA	69.91 ± 32.13	60.05 ± 33.46	63.41 ± 37.66	0.313
60 mA	74.97 ± 28.87	71.84 ± 33.49	69.57 ± 33.04	0.837
65 mA	78.41 ± 26.71	79.68 ± 31.63	73.52 ± 31.10	0.714
70 mA	82.79 ± 24.05	82.33 ± 30.66	81.54 ±25.97	0.917
75 mA	85.25 ± 22.57	85.38 ± 29.75	82.92 ± 25.39	0.827
80 mA	87.17 ± 21.98	86.45 ± 29.25	88.28 ± 20.52	0.531
85 mA	89.06 ± 20.68	92.45 ± 20.01	90.14 ± 18.75	0.647
90 mA	90.53 ± 18.58	93.35 ± 19.25	91.09 ± 18.13	0.792
95 mA	92.43 ± 16.91	94.77 ± 18.55	92.28 ±16.40	0.680
100 mA	93.74 ± 15.91	95.04 ± 18.49	92.33 ± 16.67	0.565

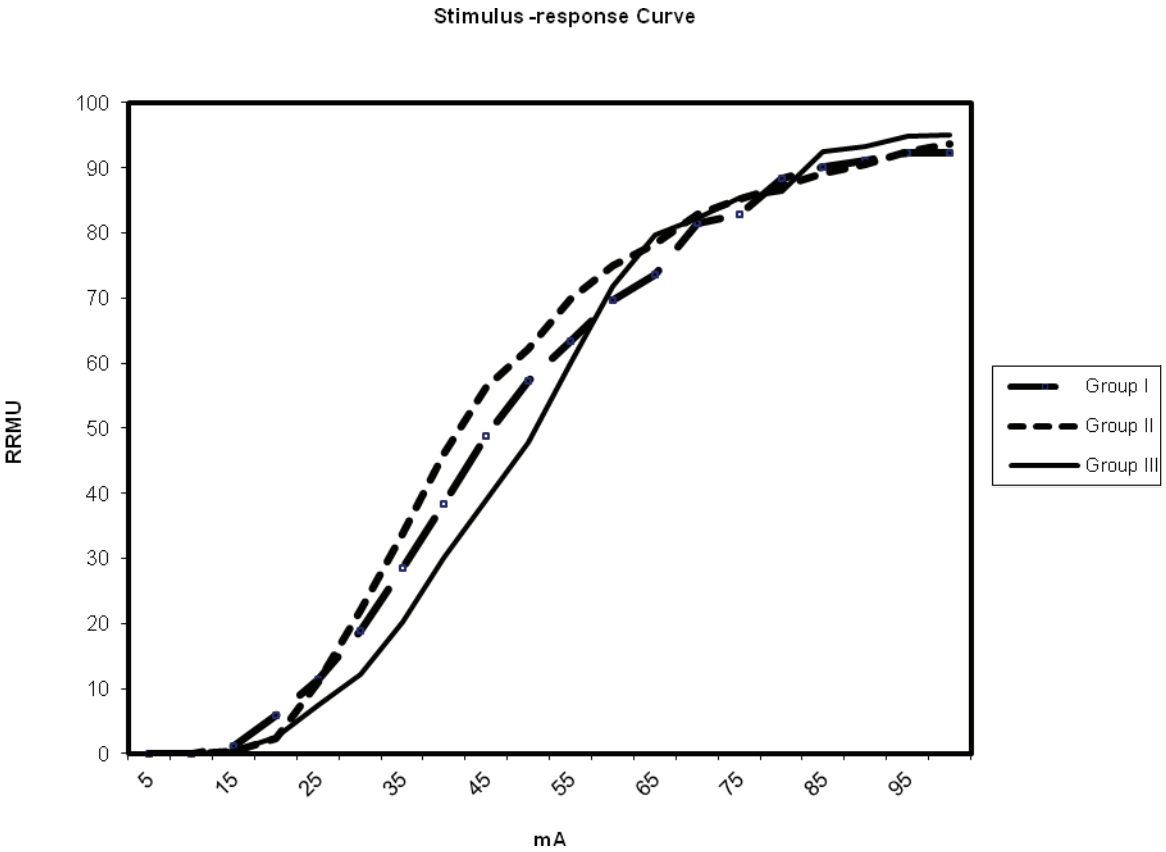

Figure 1. Stimulus-response curve for each group.

Discussion

Determination of motor latency or motor conduction velocities can be in normal limits in subclinical diabetic polyneuropathies. Regeneration or collateral sprouting in peripheral neuropathy can result axonal hyperexcitability probably due to over expression of sodium channels [7], therefore some pathological axons have lower threshold. Moreover, hyperglycemia leads to persistent sodium currents and thereby higher threshold [7, 8]. Diabetic polyneuropathy therefore has a complex pathophysiology and threshold currents can be affected by structural and metabolic changes. Detecting excitability changes in motor units with sub-threshold stimuli may give additional information about the degree of axonal involvement. In this study the firing threshold of tibial motor axons are studied in diabetic patients and normal subjects. The results showed that diabetes does not cause significant hypo/hyperexcitability in peripheral nerves. All of the suboptimal stimulus intensities excited a similar ratio of motor fibers in diabetic patients either with or without polyneuropathy and healthy controls.

In our study, we have included only distal symmetric sensorymotor polyneuropathy patients with diabetes. Therefore, the results may not be valid for other types of diabetic polyneuropathies. Besides, other features of the excitability can be observed with a greater patient group, but we did not observe a significant slope difference.

In conclusion, giving sub-treshold stimuli with increasing currents do not give additional information in determining subclinical motor nerve impairment in diabetic patients.

Disclosure or Disclaimer: The authors declare no potential conflicts of interest.

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