Introduction

Diabetic polyneuropathy is a complex set of clinical syndromes, which deplete various regions of the nervous system. The process leading to diabetic neuropathy is multi-factorial. Its symptoms are paresthesia, dysesthesia and pain. The signs of damage to the peripheral neurons are hypoesthesia, hypealgesia, hyperesthesia and hyperalgesia, decreased tendon reflexes, and, possibly, weakness and muscle atrophy. There is no universal classification. Electromyoneurography is indispensable in the diagnosis of diabetic polyneuropathy. However, there is no agreement on the most sensitive parameter for an early diagnosis. One hundred patients with diabetes mellitus were examined in order to investigate the sensitivity of different electromyographic parameters. Electromyographic techniques proved to be entirely sensitive for the early diagnosis of diabetic polyneuropathy. Some of the parameters are more suitable for an early detection of peripheral nerve damage, and others, which are not so sensitive but easy to use and stable, are suitable to follow up the course of diabetic polyneuropathy.

Key words: Diabetic Neuropathies; Signs and Symptoms; Electromyography; Early Diagnosis; Sensitivity and Specificity

Pathophysiology of diabetic polyneuropathy

In agreement with the results of retrospective and prospective studies suggesting a strong association between hyperglycemia and the development and severity of diabetic polyneuropathy (DPN), its prevalence is highest among people with poorly controlled diabetes. Until recently, there were two theories explaining the mechanism of diabetic neuropathy – metabolic and vascular. It seems most probable, however, that an interaction between the two mechanisms leads to neuropathy [8]. More recently, it has become generally recognized that the process leading to diabetic neuropathy is multi-factorial [9], although dominated by metabolic factors involving the polyol pathway and vascular disorders. Other factors that are related to those previously mentioned, such as accumulation of end-products of non-enzymatic glycosylation in the nerve and blood vessel proteins have also been recognized [10]. Furthermore, decreased n-6-essential fatty acids and prostaglandin result in damage to the nerve sheath and microvascular and blood abnormalities. In addition, a significant role is played by nitric oxides (oxidative stress), decreased neurotrophic factors, in particular nerve growth factor but also neurotrophin–3 and insulin-like growth factor, which affects axonal transport, decreased protein kinase C activity and immunological factors. Laminin has also been frequently
implicated lately. Laminin, a large heterotrimeric protein of basement membranes, appears to have a significant role in the nerve regulation and manifestations of neuropathy [11]. It promotes neurite extension in cultured neurons. An abnormal expression of laminin beta 2 gene (laminin is composed of one large alpha and two small beta chains – beta 1 and beta 2) may contribute to the pathogenesis of diabetic neuropathy.

**Clinical picture of DPN**

The most common symptoms of DPN are paresthesias and dysesthesias, which are described as feelings of walking on water, or cotton or wool strokes over the soles, or similar. Cramps are also common and usually occur in the lower leg, in particular the calf and toe flexors. Pain is usually described as sudden and poignant pain resembling piercing by a sharp tool, but also as dull and tormenting, as if holding legs in the freezing cold water [12]. It may occur at any stage of disease and is difficult to objectify. By its characteristics, this small fibre pain has all characteristics of neuropathic pain. Due to its unpleasant manifestations with the paresthetic sensations, and dysesthesias, and hyperalgesia. Decreased tendon reflexes, almost invariably the Achilles reflex, occur subsequently or simultaneously. Muscle paresis and atrophies, more often in the lower extremities, occur in advanced disease. These signs are followed by the signs of vegetative neuropathy, but the latter is not discussed in the present paper.

**Classification of diabetic neuropathy**

Recognition of various clinical syndromes of peripheral neuron damage and their likely overlapping prevents us from adopting a universal classification. There have been many attempts at systematizing different manifestations, using different criteria, both clinical and topographic, as well as subclinical, morphometric and neurophysiological signs of peripheral nerve damage. This has produced a great number of classifications of diabetic neuropathy. However, there are classifications that are widely accepted, such as Thomas’ classification [10], which differentiates between diffuse symmetrical polyneuropathy on one hand, and focal and multifocal neuropathy on the other. This classification includes also the criterion of intensity (subclinical and clinical). This practical classification with minor adaptations comprises the following:

**Subclinical neuropathy**

Rapid reversible phenomena:
1) Distal sensory symptoms
2) Reduced nerve conduction velocity
3) Resistance to ischemia-associated conduction disturbances

**Clinically manifest neuropathy**

Focal and multifocal neuropathy:
1) Cranial neuropathy
2) Thoracoabdominal neuropathy
3) Focal neuropathy of the extremities
4) Motor asymmetric neuropathy of the proximal part of lower extremities (diabetic amyotrophy)

**Electromyoneurography in the diagnosis of diabetic neuropathy**

The foundations of clinical electromyography were laid by Buchthal and Clemmesen in 1941 [13]. However, this electrophysiological technique, including peripheral nerve studies in diabetic patients, has become more widely used only in the last decades. Early studies focused on the analysis of electromyographic findings, i.e., firing patterns. In diabetic neuropathy, the pattern is usually thin and there is an increased percentage of polyphasic potentials. However, a significantly more sensitive parameter is the nerve conduction velocity study, including both sensory and motor nerve fibres, which belongs to the domain of conventional electromyography. Compared to diabetics with no clinical signs of neuropathy, in diabetics with signs of neuropathy, motor conduction velocities are more decreased and reduction of the evoked potential amplitude occurs earlier [14]. Tibial and peroneal nerves show more abnormality than ulnar and medial nerves, i.e., the lower extremities are more sensitive to diabetic damage than the upper extremities. The involvement of peripheral nerves is diffuse, more distal than proximal parts. However, some authors have long considered that distal latency in axonal neuropathies, including diabetic neuropathy, does not reflect only dysfunction of the distal segment. Namely, the loss of alpha motor neurons leads firstly to decreased motor electric conduction velocity in the distal part of the peripheral nerve. Sensory conduction velocity is considered a more sensitive study than the motor conduction velocity [15]. Burke et al. consider that sensory conduction velocity study of the sural nerve is the most sensitive electrophysiological method for the detection of polyneuropathy. More recently, sophisticated techniques for studying late responses, including F wave and H reflex, have been used. The diagnostic value of these electrophysiological parameters, especially of F wave, has been reported by many authors [16-18]. F wave is a late response widely used in clinical practice. It was first described in the annals of Johns Hopkins hospital
by Magladery and McDougal in 1951. At first, it was considered to be a polysynaptic reflex, but soon it was proved to be centripetal discharge of alpha motor neurons following antidromic stimulation of the motor fibres. This response reflects the interaction between the anterior horn cells and the possibility of afferent and efferent conduction through the motor fibres, providing information on the function of the whole pathway of the peripheral motor neuron. The fact that the pathway is used for inward and outward conduction indicates a range of parameters in both healthy individuals and patients with diseases of the peripheral nervous system. Although the minimal F wave latency is most frequently used for clinical applications, there are authors who consider chronodispersion (CHRD), i.e. the difference between the minimal and maximal latencies, the most sensitive parameter in neurophysiological studies of diabetic neuropathy [19]. The same author (Tojokura, 1998.) termed F wave chronodispersion $F_{\text{duration}}$. He found abnormal values of F wave chronodispersion in patients with normal F wave latencies. Conversely, in 1989 [17] Bernbaum et al. preferred a study of H reflex in the electrophysiological diagnosis of diabetic polyneuropathy. The latter method enables a better insight into the condition of peripheral neurons, providing information on the reflex activity and thus enabling the evaluation of the function not only of the peripheral nerve but also of superior spinal areas. As early as 1918, Paul Hoffmann described a reaction that was named after him $H$ reflex. Much later, this reaction was analyzed and applied in the practice. Today it is well known that H reflex is a result of the sensory fibre stimulation by low-voltage impulses which are transmitted by fibres from motor spindles and which, after monosynaptic delay, lead to generation of action motor potential in the cells of the anterior horn and their propagation into the muscle tissue within certain motor units. Although accepted as a highly sensitive sign of S1 radiculopathy, it has recently been used also in the study of demyelinating diseases as well as diabetic neuropathy.

**Material and methods**

We studied a hundred patients with diabetes mellitus lasting for over a year. The firing pattern, motor conduction velocity and distal latency were analyzed as parameters of the function of proximal and distal parts of peripheral motor neurons, in addition to sensory conduction velocity and the late responses H reflex and F wave in two modalities - minimal latency (F min) and chronodispersion of F waves. The results were compared with the reference values and classified into normal or abnormal ones accordingly. A higher percentage of abnormal findings of an electromyographic parameter found in the patient population indicated a greater sensitivity of the parameter in the early diagnosis of diabetic polyneuropathy.

**Results and Discussion**

We found around 73% of abnormal firing patterns in our study sample. Among these, 56% of patients had the abnormal motor conduction velocity in the distal part and 40% in the proximal part of the peripheral motor neuron. The abnormal sensory conduction velocities were found in 94% of subjects. The abnormal CHRD was found in 93% and abnormal minimal F in 59%. H reflex was abnormal in 82% of our subjects.

The most sensitive electromyographic parameter for the early detection of polyneuropathy was clearly sensory conduction velocity (SCV), which can be explained by a smaller diameter of the sensory fibres and their higher sensitivity to various endogenous and exogenous influences. On the other hand, considering the early damage to these fibres, which is often an irreversible process, this method is not suitable for the follow up of the changes in neurogenic lesions. A surprising sensitivity, i.e. a high percentage of abnormal findings, was recorded with CHRD, which was shown a reliable method for the early detection of diabetic polyneuropathy. However, the pronounced inconsistency of this F wave modality may be a factor limiting the precise detection. On the other hand, although not nearly so sensitive in the early detection, F min is a reliable parameter for following up the course of polyneuropathy. H reflex showed a significant sensitivity and is an important indicator of the function of the whole population of the nerve fibres involved in the reflex arc, from sensitive, via transmitters in the spinal cord, to the motor nerve fibres. It could also be a suitable parameter to follow up the course of diabetic polyneuropathy.

**Conclusion**

The extremely high percentage of subjects with diabetic polyneuropathy found in our study indicates the necessity of applying electromyographic techniques in the evaluation of diabetic patients before the onset of clinical symptoms and signs of neuropathy. Whereas some of the electromyographic parameters are more suitable for the early detection of peripheral nerve damage, others, which are not so sensitive but easy to use and stable, are suitable to follow up the course of diabetic polyneuropathy.
References

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Uvod

Dijabetesna polineuropatija kompleksan je skup kliničkih sindro-ma koji oštećuju različite regije nervnog sistema, bilo pojedinačno ili kombinovano. Ona je najčešća i najneprijatnija komplikacija dijabetesa, vodi velikom morbiditetu i mortalitetu i rezultira velikim ekonomskim troškovima. U poslednje vreme je opšteprihvaćen stav da je proces koji dovodi do dijabetesne neuropatije multifaktorski, iako u njemu dominiraju metabolički faktori s poremećajem poliolskog puta i vaskularni poremećaji. Simptomi su parestezije, dizestezije i bol. Znaci oštećenja perifernog nerva su hipoestezija, hipoalgezija, hiperestezija i hiperalgezija, kao i sniženje tetivnih refleksa, te eventualno slabost i atrofija mišića.

Materijal i metode

U istraživanju je, pomoću raznih elektromiografskih metoda, ispitivano stotinu bolesnika s dijabetesom melitusom u trajanju od preko godinu dana. Rezultati i diskusija

Ispitivanje je izvedeno s više elektromioneurografskih tehnika koje su se pokazale senzitivnim, a neke, zbog osetljivosti i postojanosti odgovara, i neophodnim u ranoj detekciji i praćenju toka dijabetesne polineuropatije.

Zaključak

Elektromioneurografija se u celini pokazala neophodnom u ranoj detekciji i praćenju dijabetesne polineuropatije.