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Neuropathy in young diabetic patients

Neuropatia młodych pacjentów z cukrzycą

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ABSTRACT

Diabetic neuropathy is one of the most common and serious complications of both type 1 and type 2 diabetes. In type 1 diabetes mellitus, neuropathy usually takes form of distal symmetric polyneuropathy (DPN) and/or diabetic autonomic neuropathy (DAN). Other forms such as acute sensory neuropathy, cranial neuropathy, truncal radiculoneuropathy or proximal motor neuropathy are present sporadically in those patients. There are three hypotheses that explain the pathogenetic mechanism of polyneuropathy: metabolic, vascular and immunological. Many diabetic patients have demonstrable abnormalities of autonomic neurological function without any evidence of clinical disease. Tests of autonomic function and tests of conduction velocity in peripheral nerves are assumed to be a measure of neurological state and may be important methods of assessing the therapy of diabetic complications. When it comes to therapeutic management, good metabolic control is essential for the prevention of diabetic neuropathy and remains the key element of treatment. Other methods (*e.g.* pharmacological) are used for the management of symptoms and are rarely used in the juvenile population.

Introduction

The most common form of diabetes in young patients is type 1 diabetes [1]. As the association between diabetes mellitus and neuropathy has been recognized for well over 100 years, it is not surprising that damage to the peripheral nervous system has also been documented [2]. The first reports of neuropathy in children with diabetes already appeared in the middle of the last century. Later studies were based on broader material and included, among others, the nervous conduction velocity tests [3].

Diabetes is the most common cause of neuropathy in United States and neuropathies are the most common complication of diabetes mellitus, affecting up to 50% of patients with type 1 and type 2 diabetes mellitus [4].

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Great advances in the treatment of type 1 diabetes that have been made in the last 20 years mean that chronic complications of the disease appear later than they used to. However, even the most careful treatment cannot completely eliminate the risk of their occurrence. Although overt diabetic neuropathy is rarely present in children and adolescents with diabetes, subclinical diabetic neuropathy has been estimated to occur in approximately half of all children with type 1 diabetes with a disease duration of 5 years or longer. In addition, up to 25% of pediatric patients with newly diagnosed diabetes have abnormal findings on nerve conduction studies [5].

In diabetic patients, the risk of DPN (distal symmetric neuropathy) and autonomic neuropathy can be reduced with better glycemic control and the improvement of lipid and blood pressure indexes [6–9].

Definition and classification

Diabetic neuropathy (DN) is defined as "the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes" [2, 10–13]. It is a common complication of diabetes mellitus which requires a multifactorial approach to clinical assessment since diabetes mellitus is associated with many different neuropathic syndromes [2, 14–16].

The spectrum of diabetes mellitus-associated neuropathies is large and our knowledge of these syndromes continues to evolve. Two main types are usually distinguished, named as sensorimotor and autonomic neuropathies. Sensorimotor neuropathy is characterized by pain, paresthesia and sensory loss while autonomic neuropathy causes a constellation of symptoms and signs affecting the cardiovascular, urogenital, gastrointestinal, pupillomotor, thermoregulatory and sudomotor systems [17–20]. It is important to bear in mind that autonomic neuropathy may also contribute to myocardial infarction, malignant arrhythmia and sudden death [7].

In currently proposed classification of diabetic neuropathy, the following can be distinguished [10]:

1. Generalized symmetric polyneuropathies
   a) acute sensory
   b) chronic sensorimotor
   c) autonomic
2. Focal and multifocal neuropathies.

Focal and multifocal neuropathies are typical for diabetes in the elderly and occur extremely rarely in children and adolescents – therefore they will not be addressed in this article.

Acute sensory neuropathy (acute painful neuropathy)

This form, manifesting itself with pain and paresthesia, develops in the early stage of diabetes mellitus, sometimes directly after the implementation of insulin therapy. This syndrome may associate itself with considerable loss of body weight and depression. The mechanisms underlying the development of this syndrome are still unclear [21]. Its occurrence in young patients is only occasional.

Chronic sensorimotor polyneuropathy – distal symmetric polyneuropathy (DPN)

Sensory diabetic neuropathy, determined by nerve conduction studies, is common in children with type 1 diabetes but is rarely diagnosed because of its lack of symptoms. Höliner et al. [22] found that DPN is highly prevalent in children and adolescents with type 1 diabetes mellitus but subclinical in the majority of patients. Additionally, Moser et al. [23] conducted a study which suggested that DPN can occur in young children, with short diabetes duration, and good diabetes control.

The American Diabetes Association (ADA) recommends screening for DPN in children and adolescents at diagnosis (in type 2 diabetes) or 5 years after diagnosis (in type 1 diabetes), followed by annual evaluations thereafter, using simple clinical tests [6]. Screening is required in order to identify subclinical signs of DPN in its earliest stages.

Recently, Hirschfeld et al. [24, 25] analyzed the usefulness of certain diagnostic tests to screen for diabetic peripheral neuropathies (DPN) in children and adolescents. They demonstrated that diagnostic accuracy was heterogeneous for the different screening methods. Acceptable performance was demonstrated for the biothesiometer and the monofilament in detecting DPN in children and adolescents compared with the gold standard nerve conduction studies. According to the authors, the problem of reliability needs to be more thoroughly addressed in order to improve the screening procedures in diabetes management.

Nerve conduction studies (NCS) are the gold-standard for the detection of subclinical DPN – however, it is an invasive method. Thermal discrimination thresholds (TDTs) and vibration sensation thresholds (VSTs) are quicker, easier and, therefore, more suitable as screening tools [26]. Blankenburg et al. [27] think that quantitative sensory testing (QST) is a valuable tool for the assessment of neuropathy as well as a target of interventional studies in children with diabetes.

On the other hand, the neuropathy disability score (NDS) has been evaluated as a possible alternative method for measuring DPN. For example, Weintrob et al. [28] compared it to QST and found it to have better correlation with glycemic control and microvascular complications. Such performance, in the scope of easy access and cost-effectiveness, would make NDS the preferred method of evaluating neuropathy in young patients.

The most common of the diagnostic methods mentioned above and in the further parts of this article will be described in more detail in the "Examinations" section.

Diabetic autonomic neuropathy (DAN)

Diabetic autonomic neuropathy may develop as one of two categories: