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Methods for assessing selected disorders of the autonomic nervous system in neurodegenerative diseases

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Abstract

Neurodegenerative diseases belong to the group of progressive disease entities leading to pathological changes in nerve cells. Loss of nerve cells causes numerous motor and non-motor disorders, which include autonomic nervous system (AUN) disorders.

The aim of the study is to review the available literature on the most frequently occurring disorders of the autonomic nervous system occurring in neurodegenerative diseases and methods of their diagnosis. For this purpose, databases such as MedLine, PubMed, Cochrane Library and Polish Medical Bibliography were searched. Articles in Polish and English were selected.

The paper presents the methods most commonly used to assess the autonomic nervous system, cardiovascular disorders. Accounted for methods that, thanks to their ease of implementation, have found wide clinical application. Non-invasive methods include, among others: analysis of heart rate variability, 24-hour blood pressure monitoring, tilt test and deep slow breathing test. In addition to the above-mentioned studies and tests, the literature also includes questionnaires for assessing dysautonomy. The most commonly used is the Iowa

Autonomous Symptom Questionnaire.

Studies published so far confirm the need to use AUN assessment in neurodegenerative diseases. Diagnosis and treatment of nervous system dysautonomics is important from the point of view of a holistic therapeutic approach.

Key words: multiple sclerosis, parkinson disease, autonomic dysfunction, dysautonomy

Introduction

Neurodegenerative diseases belong to the group of progressive disease units of the nervous system, which result in pathological changes in nerve cells. This group of patients includes people suffering from multiple sclerosis or Parkinson's disease. Pathological loss of nerve cells causes numerous motor and non-motor disorders, including disorders of the autonomic nervous system. The autonomic nervous system (ANS) is responsible for maintaining the homeostatic balance of the body, depending on the activity of such systems as: cardiovascular, respiratory, digestive, and thermoregulation [1, 2].

Multiple sclerosis (MS) is a chronic disease of the central nervous system with an autoimmune background, classified into the group of demyelinating disorders. The disease is more often diagnosed in women. The number of patients in Poland is not well known, there is no register and the Polish Society of Multiple Sclerosis only provides estimated numbers of patients. The course of MS is different, therefore the clinical forms of the disease are distinguished: secondary-progressive and relapsing-remitting, primary-progressive and benign. Parkinson's disease (PD) is a long-term degenerative disorder of the central nervous system and it mainly affects the motor system. The symptoms usually emerge slowly. Early in the disease, the most obvious symptoms are shaking, rigidity, slowness of movement, and difficulty with walking. As the disease worsens, non-motor symptoms become more common [1, 2, 3].

The symptoms of involvement of the ANS are often non-specific, hence the need for a comprehensive assessment of the autonomous system is emphasized in the scientific literature. Clinical and electrophysiological tests should be performed in patients with suspected ANS [3].

Methods for assessing ANS involvement in the cardiovascular system

The assessment of dysautonomy consists in a detailed analysis of the subjective and subjective symptoms indicating the involvement of the autonomic nervous system [3].

An interview is an important tool in subject research. It should include questions about the most common symptoms of dysautonomy. Including dizziness, tinnitus, a feeling of "darkness in front of the eyes" that appear after getting up quickly from a lying or sitting position, or after standing for a long time indicate orthostatic disorders. These symptoms can be caused by orthostatic hypotension, which is often the first symptom of dysautonomy. On the other hand, symptoms occurring after upright position, such as tachycardia, palpitations, headache, dizziness, nausea, anxiety, and less often fainting, may indicate postural orthostatic tachycardia syndrome [4].

The quantitative assessment of the signs and symptoms of dysautonomia is facilitated by the use of questionnaires, such as, for example, the Autonomic Symptom Profile [5], Composite Autonomic Scoring Scale (CASS) [6]. In Poland, the frequently used questionnaire is the Autonomic Symptom Questionnaire developed by Lova et al. [6]. Questions about ANS dysfunctions are divided into those regarding cardiovascular disorders, including orthostatic disorders, and other systems: secretory, excretory, digestive system. In addition, pupil width regulation disorders, as well as sleep and sexual dysfunction [Tab.1].

In patients with orthostatic hypotension, cardiac arrhythmias are found in the Valsalva trial (maneuver) - involving an intensive exhalation with the glottis closed, lasting 15 seconds. This test is commonly used to assess the efficiency of autonomic regulation in the cardiovascular system. The Valsalva maneuver leads to a short-term decrease in blood pressure, and compensatory reactions restoring normal blood pressure are mediated mainly by a reflex from arterial baroreceptors. On this basis, the Valsalva maneuver is considered one of the methods of assessing the sensitivity (sensitivity) of arterial baroreceptors, it is a parameter of dysfunction of the parasympathetic system. In people with Parkinson's disease a significant weakening of cardiovascular baroreceptor response can be observed [3].

In addition, the majority of patients with orthostatic hypotension showed a significant reduction of left ventricular noradrenergic sympathetic innervation. Myocardial SPECT, which is a tomographic technique in which any cross-sectional distribution of radioactivity in the myocardium is obtained using a computer, using ¹²³I-metaiodobenzylguanidine - a precursor of noradrenaline - a decrease in radioactivity in the myocardium, indicating a sympathetic dysfunction involving fibers postganglionic. Due to the limited availability of cardiac scintigraphy in patients with cardiovascular disorders, it is advisable to perform tests assessing autonomic functions such as 24-hour blood pressure monitoring and upright test [3, 7].

Tabela 1. Autonomic Disorder Questionnaire modified according to Low et al.[6].

DYSAUTONOMY SYMPTOMS according to Low	Severity of symptoms (in points)
Orthostatic disorders (including dizziness)	0-4
Angioedema (e.g. discoloration and skin warming)	0-1
Secretory symptoms (including excessive sweating)	0-1
Post-exercise symptoms (including nausea, vomiting, anorexia)	0-3
Stomach pain	0-1
Diarrhea	0-1
Persistent constipation	0-1
Bladder dysfunction (including urinary incontinence or retention)	0-1
Sexual dysfunction (e.g. loss of libido, erectile dysfunction / ejaculation)	0-1
Sleep disorders (e.g. snoring, apnea)	0-1
Blurred vision	0-1
Accompanying diseases and medications used affecting the function of the autonomic system	0-1
Physical examination	
Blood pressure and pulse measured in the supine, standing and squat position	0-2
Post-secretion symptoms	0-1
Angioedema symptoms	0-1
Pupillary symptoms	0-1

After 24-hour blood pressure monitoring, patients with Parkinson's disease were shown to have abnormalities in the normal blood pressure profile with hypertension at night and a significant reduction in pressure during the day and after meals. Cardiovascular disorders are more common in patients in the advanced period of this disease [8].

The tilt test consists of performing passive uprighting using a verticalising table. In the study by Jaipurkar et al. [9], he compares responses to orthostatic stimuli in the Parkinson's group and healthy people. Symptoms indicative of autonomic nervous system dysfunction occurred in 65% of patients with Parkinson's disease. In the study of Studer et al. [10] patients with multiple sclerosis were upright to an angle of 65°. The standing up took 10 minutes. Autonomic imbalances were found in patients suffering from progressive MS, showing a predominance of sympathetic activity at rest. It has also been observed that the severity of the disease significantly affects the ratio of sympathetic-parasympathetic balance factor LF (low-

frequency component) / HF (high-frequency) [10]. In another study by Damla et al. conducted an analysis of heart rate variability using 24-hour Holter monitoring. The study compared the results of 51 patients with multiple sclerosis diagnosed with relapsing-remitting form and 44 healthy people. The study showed that heart rate variability values were significantly lower in patients with multiple sclerosis compared to the control group [11].

Electrophysiological diagnostics of autonomic system function is another AUN research method. It involves performing two non-invasive tests - sympathetic skin response (SSR) and heart rate variability (HRV) analysis [12, 13].

HRV analysis allows you to assess the balance between the sympathetic and parasympathetic parts in the cardiovascular system. In this case, physiological phenomena are used, such as accelerating the heart rhythm during inspiration and slowing down during exhalation, i.e. respiratory irregularity, as well as changes in sinus rhythm after uprighting. R-R intervals during deep breathing and at rest are analyzed. In HRV assessment, the non-parametric method based on Fourier transformation is most commonly used [14]. Currently, spectral analysis of heart rate variability (in the frequency range) is also possible. The following components are evaluated for the analysis of total spectrum power:

- HF - *high frequency* (0,15-0,4 Hz), describes changes associated with parasympathetic activity, breathing and changes in blood pressure,
- LF - *low frequency*) (0,04-0,15 Hz), describes changes modulated by the sympathetic nervous system, probably also includes changes related to baroreceptor activity,
- VLF - *very low frequency* (< 0,04 Hz), associated with chemoreceptor and baroreceptor activity [14].

The simplest and most commonly used test for assessing the ANS is the deep breathing test (DBT). He mainly examines the parasympathetic component of autonomic innervation. It consists of deep breathing at a rate of 6 breaths per minute controlled to facilitate the metronome for 3 minutes. The maneuver increases the systolic chest pressure with a simultaneous change in the length of the R-R intervals. The test mainly causes a change in the parasympathetic reflex part of the autonomic system, both its inhibition and activation. Bidikar et al. [15] conducted a 3-minute deep breathing test in the study of dysautonomy in Parkinson's disease. It was found that DBT was abnormal in 40% of cases, while the borderline result was obtained in 33.3% of patients and normal in 26.6% of patients with Parkinson's disease [15].

The autonomic imbalances were found in patients suffering from progressive MS. The predominance of sympathetic activity at rest was found. Flachenecker [16] conducted a study of 40 MS patients for cardiovascular disorders and orthostatic intolerance. The methods for assessing the parasympathetic part (pulse response to the Valsalva maneuver, deep breathing test and active change in posture), as well as sympathetic function tests (blood pressure responses to active posture change), and spectral analysis of heart rate variability during rest and upright position were used. The obtained results were compared with the results obtained in a healthy control group. Abnormal cardiovascular responses in at least one of the tests were observed in 40% of patients with multiple sclerosis, compared with 17% of the control group. Orthostatic intolerance was reported in 50% of patients, while only 14% of healthy subjects reported symptoms of orthostatic intolerance [16].

Conclusions

Assessment of the functions of the autonomic system, which is involved in neurodegenerative diseases, is important from a practical point of view. It will help detect life-threatening dysautonomies. Electrophysiological tests are performed to differentiate neurodegenerative diseases. In addition, when analyzing the function of the ANS in patients with pathology of the nervous system, it is necessary to take into account the functions of side disorders. In patients with Parkinson's disease, autonomic functions are impaired at different levels, both in the sympathetic and parasympathetic parts of the ANS. Early diagnostics of dysautonomy, including the cardiovascular system, can help identify a group of patients who are particularly vulnerable to vascular complications. Orthostatic disorders are the most common and often the first symptoms on the part of the ANS in patients with neurodegenerative disease. These include dizziness, nausea, palpitations, dark spots before the eyes, appear after changing the position from horizontal to vertical.

The research published above confirms the need for ANS assessment in neurodegenerative diseases. Diagnosis and treatment of dysautonomy of the nervous system is important from the point of view of holistic therapeutic approach and effect.

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