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CASE REPORT OF PARKINSON'S DISEASE AND ORTHOSTATIC HYPOTENSION

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SUMMARY

Introduction: Parkinson's disease is an idiopathic, slow progressive neurodegenerative condition with the loss of dopaminergic neurons in the substantia nigra compacta of the midbrain. Due to cardiovascular dysautonomia and impaired baroreflex function in Parkinson's disease, the development of orthostatic hypotension is most common, along with increased blood pressure variability, supine hypertension, nocturnal hypertension, etc. Orthostatic hypotension in Parkinson's disease increases the risk of developing coronary heart disease, myocardial infarction, and the risk of overall, and cardiovascular mortality.

Case report: Orthostatic hypotension in Parkinson's disease is associated with an increased risk of gait disturbances, loss of balance, falls resulting in injuries and limb fractures, and mortality. In this paper, we presented a patient who had previously been treated for arterial hypertension, with the current clinical presentation of symptomatic orthostatic hypotension in Parkinson's disease. After neurological evaluation and the implementation of pharmacological and non-pharmacological therapy for orthostatic hypotension, gradual improvement and stabilization of blood pressure values are achieved, along with a reduction in orthostatic hypotension symptoms and a decrease in subjective discomfort.

Conclusion: In the presence of orthostatic hypotension in Parkinson's disease, in addition to pharmacological therapy, non-pharmacological treatment measures are very important for stabilizing blood pressure values and reducing the symptoms of orthostatic hypotension.

Keywords: Parkinson's disease, orthostatic hypotension, autonomic dysfunction, blood pressure, falls

SRPSKI

SAŽETAK

Uvod: Parkinsonova bolest je idiopatsko sporo progresivno neurodegenerativno oboljenje sa gubitkom dopaminergičkih neurona u kompaktnom delu substancije nigre međumozga. Usled kardiovaskularne disautonomije i narušene funkcije barorefleksnog luka kod Parkinsonove bolesti dolazi do razvoja najčešće ortostatske hipotenzije, zatim povećane varijabilnosti krvnog pritiska, hipertenzije u ležećem položaju, noćne hipertenzije itd. Ortostatska hipotenzija kod Parkinsonove bolesti povećava rizik od nastanka koronarne bolesti srca, infarkta miokarda, i rizik od ukupnog i kardiovaskularnog mortaliteta.

Prikaz bolesnika: Ortostatska hipotenzija kod Parkinsonove bolesti povezana je sa povećanim rizikom od poremećaja hoda, gubitka ravnoteže, padovima sa povredama i prelomima ekstremiteta i mortalitetom. U ovom radu smo prikazali bolesnika koji se ranije lečio od arterijske hipertenzije, sa aktuelnom kliničkom slikom simptomatske ortostaske hipotenzije kod Parkinsonove bolesti. Nakon neurološke obrade i uključivanja farmakološke i nefarmakološke terapije ortostatske hipotenzije, postiže se postepeno poboljšanje i stabilizacija vrednosti krvnog pritiska, redukcija simptoma ortostatske hipotenzije i smanjenje subjektivnih tegoba.

Zaključak: Kod postojanja ortostatske hipotenzije kod Parkinsonove bolesti pored farmakološke terapije, nefarmakološke mere lečenja su veoma značajne za stabilizaciju vrednosti krvnog pritiska i redukciju smiptoma ortostatske hipotenzije.

Ključne reči: Parkinsonova bolest, ortostatska hipotenzija, autonomna disfunkcija, krvni pritisak, padovi.

INTRODUCTION

The first detailed description of Parkinson's disease was provided by the British physician James Parkinson in 1817. Today, Parkinson's disease is defined as an idiopathic, slow progressive neurodegenerative condition with the loss of dopaminergic neurons in the compact part of the substantia nigra of the midbrain. It is characterized by the accumulation of abnormally phosphorylated α-synuclein, and aggregates are typically found in neurons as Lewy bodies. A reduction in dopamine levels and an increase in acetylcholine in the brain lead to the appearance of motor symptoms such as resting tremor, rigidity, bradykinesia, and postural instability, as well as non-motor symptoms including depression, dementia, sleep disorders, and autonomic dysfunction (1,2). The prevalence of Parkinson's disease is not well known, but it is estimated to be around 1-3% in the general population. It is more commonly observed in men over the age of 65, Caucasian, and in economically developed countries (3). Large clinical studies have shown that patients with Parkinson's disease have an increased risk of developing myocardial infarction, ischemic stroke, heart failure, and sudden death (4).

Autonomic dysfunction is present in all stages of the disease, but typically prevalence in the advanced stages of the disease. Cardiovascular autonomic dysfunction and impaired baroreflex function in Parkinson's disease are most commonly characterized by the occurrence of neurogenic orthostatic hypotension, increased blood pressure variability, supine hypertension, postprandial hypotension, nocturnal hypertension, etc. Long-term blood pressure abnormalities, as well as chronic arterial hypertension, can lead to serious adverse cardiovascular and cerebrovascular events, including stroke (5,6).

Neurogenic orthostatic hypotension, as the most common manifestation of autonomic dysfunction in Parkinson's disease, occurs in 30-78% of patients (7). Orthostatic hypotension is defined as a decrease in systolic blood pressure of ≥20 mmHg and a decrease in diastolic blood pressure of ≥10 mmHg within 3 minutes of changing from a seated to a standing position. Systolic blood pressure values in the standing position of <90 mmHg also suggest orthostatic hypotension, and are often a precursor to symptoms of orthostatic hypotension. Cerebral hypoperfusion can lead to the development of dizziness, gait disturbances, loss of balance, falls resulting in injuries and fractures, lower back pain, blurred vision, transient cognitive impairment, and even loss of consciousness. Muscular hypoperfusion can lead to headaches, pain in the neck and lumbal region. Additionally, symptoms such as fatigue, chest pain, and difficulty breathing may also occur. Some patients may have relatively few symptoms, which occur intermittently, or they may remain asymptomatic. Postural hypotensive symptoms occur in 56% of patients with Parkinson's disease, and the frequency of these symptoms increases with the progression of the disease, significantly impairing the quality of life (8). Orthostatic hypotension in Parkinson's disease increases the risk of developing coronary heart disease, myocardial infarction, congestive heart failure, and the risk of overall and cardiovascular mortality (9).

CASE REPORT

A 74-year-old man comes for examination by a cardiologist due to frequent episodes of hypotension, with blood pressure values measured at home being 100/60 mmHg. The patient reports symptoms of fatigue, weakness, unsteadiness when walking, dizziness, and exhaustion. Denies loss of consciousness. The patient has previously been treated for arterial hypertension since 2003. The maximum recorded blood pressure values were 165/105 mmHg, and since then, they have been on regular antihypertensive therapy with one tablet of Ramipril 5 mg in the morning and one tablet of Amlodipine 5 mg in the evening. Currently, he states that he has been irregularly taking Amlodipine 2.5 mg 1x1 due to lower blood pressure values at home. Since 2015, he has been diagnosed with Parkinson's disease and is being monitored by a neurologist. Denies a family history of cardiovascular diseases.

During the auscultatory examination of the lungs, normal breath sounds are heard without any additional findings. The heart sounds are rhythmic, tones are clear, and there is a mild systolic ejection murmur at the aortic area. Blood Pressure (BP) in the sitting position was 118/65 mmHg, and heart rate (HR) was 73/min. Then, measured in the standing position: BP 95/60 mmHg, HR: 77/min, suggesting orthostatic hypotension. In the objective findings, the man is of normal weight, with a height of 181 cm and a weight of 80 kg, resulting in a BMI (Body Mass Index) of 24.4 kg/m2.

On the ECG, a sinus rhythm is recorded with left-axis deviation, rS in D3, aVF, HR: 77/min, without disturbances in heart rhythm, and no ST-T changes.

The echocardiographic examination of the heart shows a normal-sized left ventricle with an end-diastolic dimension (EDD) of 5.4 cm and an end-systolic dimension (ESD) of 3.3 cm. Global contractile function is preserved with an ejection fraction (EF) of 65% (by 2D Simpson method), without segmental contractility impairments. Myocardial thickness is normal, with a septum measuring 1 cm and the posterior wall measuring 0.9 cm. The transmitral flow indicates grade I diastolic dysfunction with an E/A ratio of 0.35 m/s. On the mitral valve, there is a minor calcification of the posterior mitral annulus. The mitral valve leaflets show preserved motion amplitude. Mitral regurgitation is detected in a trace amount.

The aortic annulus is partially calcified, with a normal lumen width of 3.2 cm. The aortic valve is tricuspid, and the cusps have preserved separation. The flow over the aortic outflow is of preserved velocity. The left atrium is enlarged in dimensions, measuring 4.6 cm from the parasternal long-axis view. The right heart chambers are of normal dimensions, with the right ventricle measuring 2.6 cm. Tricuspid regurgitation is detected in a trace amount. The right heart pressure (Pulmonary Artery Systolic Pressure - PASP) is preserved. The pulmonary artery has a normal lumen width with preserved flow. The pericardium exhibits a normal intensity of reflected echoes, with no layers and no effusion.

On a 24-hour ambulatory blood pressure monitoring, the average arterial pressure was 118/76 mmHg (HR: 66/min), during the daytime 122/81 mmHg (HR: 71/min), and during the nighttime 115/70 mmHg (HR: 60/min). The average value of mean arterial pressure was 95 mmHg (100 mmHg during the day and 90 mmHg during the night). The average value

of pulse pressure was 42 mmHg (40 mmHg during the day and 45 mmHg during the night). The maximum measured blood pressure values during the daytime were 147/106 mmHg (3:30 PM), and during the nighttime, they were 149/97 mmHg (10:03 PM). The circadian rhythm is preserved. The examination was done without therapy, previously discontinuing Amlodipine 2.5 mg 1x1 (Figure 1).

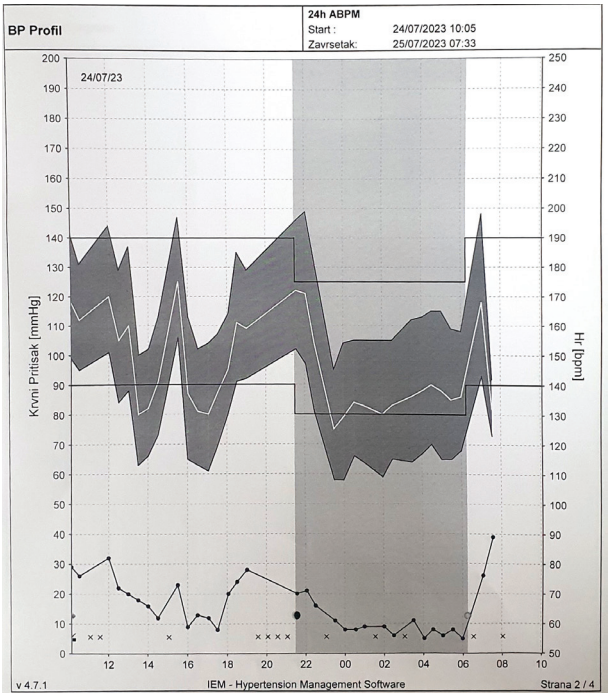

***Figure 1** - 24-hour ambulatory blood pressure monitoring*

The patient has been referred to a neurologist for an assessment regarding Parkinson's disease and for the prescription of specific therapy. The patient complains of trembling in the left hand, occasional shaking in the right hand, and instability. He has not experienced falls or injuries. In the neurological status: moderate tremor in the left hand, mild rigidity, and slight bradykinesia on the left side. Postural stability is preserved. He is currently not using any neurological therapy. In the laboratory analyses: blood count and sedimentation are within normal limits, glucose level 5.9, urea 4.3, creatinine 73, cholesterol 5.1, HDL cholesterol 1.10, LDL cholesterol 3.41, triglycerides 1.30, AST 14, ALT 12.

Based on a complete clinical and diagnostic assessment, it has been determined that the condition is neurogenic orthostatic hypotension in Parkinson's disease. During the neurologist's examination, specific therapy has been introduced to treat both the non-motor and motor symptoms of Parkinson's disease.

The patient is on the following treatment: Madopar tablets (levodopa, benserazide) 250 mg half a tablet at 7 AM, 1/4 at 11 AM, 1/4 at 3 PM, 1/4 at 7 PM, Rivotril tablets (clonazepam) 2 mg 3x1/4, Cardiopirin 100 mg 1x1 in the morning, discontinuation of antihypertensive therapy. He was advised to intake 2-2.5 liters of fluids daily, drink a bolus of water after waking up, consume a slightly saltier diet, sleep with an elevated head of the bed at night, gradually increase physical activity, reduce daytime napping, perform exercises to strengthen the lower extremities. With the introduction of pharmacological therapy and non-pharmacological treatment measures, there is a gradual improvement and stabilization of the patient's blood pressure values, reduction of orthostatic hypotension symptoms, and a decrease in subjective discomfort.

DISCUSSION

The blood pressure gradually decreases normally during the night and sleep, but in the morning at the moment of waking up, it sharply increases and then slowly decreases. The circadian rhythm of blood pressure is regulated by a series of nervous and humoral factors. The autonomic nervous system, including the sympathetic and parasympathetic nervous systems, plays a significant role in regulating the circadian rhythm of blood pressure (10). The disruption of cardiovascular homeostasis in Parkinson's disease is a complex phenomenon that arises from cardiac noradrenergic degeneration, extracardiac noradrenergic degeneration, and impaired baroreflex function. Due to the imbalance between the sympathetic and parasympathetic nervous systems and the development of cardiovascular dysautonomia in Parkinson's disease, various conditions can occur, such as orthostatic hypotension, increased blood pressure variability, supine hypertension, postprandial hypotension, exercise-induced hypotension, and nocturnal hypertension. Autonomic dysfunction in Parkinson's disease, especially blood pressure fluctuations, occurs both in the early stages of the disease and in its advanced phase (11,12).

Orthostatic hypotension is associated with a decreased quality of life and the development of a more severe form of Parkinson's disease, manifesting both motor and non-motor symptoms of the disease. Symptomatic orthostatic hypotension can lead to dramatic complications such as loss of consciousness, falls, limb fractures, head injuries, and a significant increase in the risk of mortality (13,14).

For diagnosing orthostatic hypotension in Parkinson's disease, in addition to the conventional method of measuring blood pressure, the most significant approach is the 24-hour ambulatory blood pressure monitoring (ABPM). The head-up tilt test is significant for diagnosing orthostatic hypotension, but its execution requires complex equipment, such as an electronically controlled tilt table and software (15).

The primary consequence of autonomic dysfunction in Parkinson's disease is orthostatic hypotension, which can be treated with pharmacological therapy and non-pharmacological treatment. Two drugs approved by the FDA for treating orthostatic hypotension in Parkinson's disease are midodrine and droxidopa. If patients do not tolerate or respond to the first line of therapy, fludrocortisone and pyridostigmine can be administered as an alternative. The most significant non-pharmacological measures for treating orthostatic hypotension include physical activity, intake of 2-2.5 liters of fluids daily, increased salt intake, use of compression clothing, exercises to strengthen the muscles in the lower extremities, sleeping with an elevated head of the bed, etc. (16-18).

CONCLUSION

The aim of this study is to emphasize the importance of treating orthostatic hypotension as the most common manifestation of cardiovascular autonomic dysfunction in

Parkinson's disease. In addition to pharmacological treatment, non-pharmacological therapy for orthostatic hypotension can successfully lead to stabilizing blood pressure values, reducing symptoms of orthostatic hypotension, and preventing the risk of falls resulting in injuries and fractures among patients.

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