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Cardiac autonomic neuropathy: Risk factors, diagnosis and treatment

Cardiac autonomic neuropathy (CAN) is a serious complication of diabetes mellitus (DM) that is strongly associated with approximately five-fold increased risk of cardiovascular mortality. CAN manifests in a spectrum of things, ranging from resting tachycardia and fixed heart rate (HR) to development of "silent" myocardial infarction (SMI).

The risk of developing autonomic dysfunction in DM depends on several factors. However, two of them are common to both type 1 DM (T1DM) and type 2 DM (T2DM): Degree of glycemic control and disease duration. Inadequate glucose control plays an important role in the initial pathophysiology [microcirculation dysfunction due to nitric oxide loss, oxidative stress and accumulation of free radicals with lesion of Schwann cell] as well as in its progression (neuronal apoptosis and axonal degeneration).

Clinical correlates or risk markers for CAN are age, DM duration, glycemic control, hypertension, and dyslipidemia (DLP), development of other microvascular complications. Established risk factors for CAN are poor glycemic control in T1DM and a combination of hypertension, DLP, obesity, and unsatisfactory glycemic control in T2DM.

Development of CAN is associated with reduction in heart rate variability (HRV), resting tachycardia, orthostatic hypotension (OH) and sudden death syndrome. Classification of diabetic CAN. Subclinical phase: Decreased HRV. Early phase: Resting tachycardia. Advanced stage: Excercise intolerance; Cardiomyopathy with left ventricular dysfunction; OH; SMI.

Screening for CAN should be performed in T2DM patients at diagnosis and T1DM patients after 5 years of disease, in particular those at greater risk for CAN due to a history of poor glycemic control (HbA1c > 7%), or the presence of one major CVD risk factor, or other chronic complications of DM.

Symptomatic manifestations of CAN include sinus tachycardia, exercise intolerance, OH, abnormal blood pressure (BP) regulation, dizziness, presyncope and syncope, intraoperative cardiovascular instability, asymptomatic myocardial ischemia and infarction. Symptoms compatible with orthostasis, such as feeling faint or dizzy, circumoral paresthesia may be caused by postural tachycardia syndrome, neurocardiogenic syncope, inappropriate sinus tachycardia, or abnormalities in baroreceptor function.

Methods of CAN assessment in clinical practice include assessment of symptoms and signs, cardiovascular reflex tests based on HR and BP, short-term variability, QT interval prolongation on electrocardiography (ECG), HR variability (24 h, classic 24 h Holter ECG), ambulatory BP monitoring. Additional methods are assessment of HR turbulence, baroreflex sensitivity, muscle sympathetic nerve activity, catecholamine assessment and cardiovascular sympathetic tests, heart sympathetic imaging.

Prevention of diabetic CAN focuses on lifestyle modifications and tight glucose control. Although it is common complication, the significance of CAN has not been fully appreciated and there are no unified

treatment algorithms for today. Treatment is based on early diagnosis, life style changes, optimization of glycemic control and management of cardiovascular risk factors.

Pathogenetic treatment of CAN includes: Balanced diet and physical activity; optimization of glycemic control; treatment of DLP; antioxidants, first of all α-lipoic acid (ALA), aldose reductase inhibitors, acetyl-L-carnitine; vitamins, first of all fat-soluble vitamin B1 (benfotiamine); correction of vascular endothelial dysfunction; prevention and treatment of thrombosis; in severe cases-treatment of OH.

The promising methods include prescription of prostacyclin analogues, thromboxane A2 blockers and drugs that contribute into strengthening and/or normalization of Na+, K+-ATPase (phosphodiesterase inhibitor), ALA, dihomo-γ-linolenic acid (DGLA), ω-3 polyunsaturated fatty acids (ω-3 PUFAs), and the simultaneous prescription of ALA, ω-3 PUFAs and DGLA, but the future investigations are needed.

Development of OH is associated with severe or advanced CAN and prescription of nonpharmacological and pharmacological, in the foreground midodrine and fludrocortisone acetate, treatment methods are necessary.

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