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Některé aspekty patofyziologie plicní arteriální hypertenze a její výskyt v České republice

Some aspects of pathophysiology of pulmonary arterial hypertension and its epidemiology in the Czech Republic

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Abstract

Pulmonary arterial hypertension (PAH) is a group of diseases characterized by a progressive increase of resistance and pressure in pulmonary vascular bed. In all types of PAH the same four pathological processes are reported: vasoconstriction, inflammation, thrombosis and remodelling. The genetic background is essential for the development of PAH.

We aimed to investigate the role of polymorphisms of endothelial nitric oxide synthase (eNOS) genes in PAH. We studied 142 PAH patients and 189 healthy subjects. We examined 3 polymorphisms of the eNOS gene, including the Glu298Asp polymorphism, 27-base pair (bp) variable numbers of tandem repeats (VNTR) and -786 T/C promoter gene polymorphism. Prevalence of 27-bp VNTR allele A was higher in patients with PAH compared with healthy controls. Patients with PAH associated with connective tissue diseases had higher prevalence of AA genotype compared with other PAH subgroups. The Glu298Asp polymorphism and -786 T/C polymorphism are not associated with PAH.

Thrombotic arteriopathy is an important pathophysiological feature of PAH. We analyzed fibrinogen, aPTT, INR, protein C, protein S, APC resistance, AT III, D-dimer, APA IgG, IgM APA, F VIII, vWF, t-PA and PAI in 93 PAH patients and 79 healthy controls. We aimed to demonstrate coagulation profile in diferent PAH subgroups. We demonstrated lower levels of coagulation inhibitors, elevated levels of antiphospholipid antibodies, higher levels of vWF and and increased levels of fibrinolysis inhibitors in PAH patients compared to controls. We have shown higher levels of CRP and fibrinogen in patients with PAH associated with connective tissue diseases compared to controls and impaired fibrinolysis in patients with PAH associated with congenital heart diseases.

In the final part of this study we provided estimates for epidemiological parameters of PAH in the Czech Republic. A total of 191 PAH patients diagnosed according to a standardized definition before 2007 and newly diagnosed in 2007 were entered in the national PAH registry. The prevalence and incidence of PAH in the Czech Republic were 2.24 cases/100.000 of adult inhabitants and 1.07 cases/100.000 of adult inhabitants/yr. One-year survival was 89% in the incident cohort.

Key words: pulmonary arterial hypertension, gene polymorphisms, endothelial nitric oxide synthase, thrombotic arteriopathy, epidemiology