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„Regulacja odpowiedzi zapalnej u pacjentów z niewydolnością serca w zależności od stanu klinicznego z uwzględnieniem leczenia resynchronizującego”

Summary

Chronic heart failure (CHF) results from the structural and functional cardiac abnormalities that lead to the impaired, inadequate blood supply to the tissues. This disease is a condition characterized by the high morbidity and mortality, that usually develops as a complication of the coronary artery disease, cardiomyopathy, pressure or volume overload of the heart. The development of CHF is a complex and multifactorial process and inflammatory activation is one of the mechanisms involved. Cytokines play an important role in the regulation of the inflammatory response by controlling many intracellular processes and cell interactions. They may have a detrimental or favorable impact on the heart muscle structure and function. The improvement of the knowledge about the inflammation role in CHF will allow a better understanding of the disease and may influence the effectiveness of therapy.

The aim of this study was to evaluate the association of inflammatory mediators such as interleukin-6 (IL-6), its two circulating receptors - glycoprotein 130 (sgp130), IL-6 receptor (sIL-6R), circulating tumor necrosis factor-like weak inducer of apoptosis (sTWEAK) and cluster of differentiation 163 (sCD163) with the CHF and response to cardiac resynchronization therapy (CRT) with the use of the selected functional, imaging and biochemical tests.

The study involved 88 patients with advanced heart failure confirmed by echocardiography (LVEF < 35%) (heart failure with reduced ejection fraction - HF-REF) in NYHA II-III functional class. The HF-REF etiology included ischemic heart disease or dilated cardiomyopathy. The reference population was composed of two groups without the CHF history: 35 controls - patients matched for sex, age and concomitant diseases, and 27 healthy individuals. All patients underwent echocardiography, cardiopulmonary exercise test (CPET) 6-minute walk test and venous blood tests. The concentrations of IL-6, sgp130, sIL-6R, sTWEAK and sCD163 were measured with the use of the ELISA method. Most of the patients were examined once, only 45 HF-REF patients who had implanted CRT device, were also controlled after 6 months of CRT.

The basic clinical profile of the HF-REF patients and the comorbidities matched controls had similar demographic parameters, whereas differed in terms of laboratory, echocardiographic and exercise capacity parameters. HF-REF patients had significantly higher left ventricular end-diastolic and end-systolic volume, shorter 6-minute walk distance and impaired gas exchange parameters. The study group compared to the control group demonstrated higher IL-6 and lower sIL-6R levels, while the concentration of sgp130 did not differ. After 6 months of CRT approximately 2/3 of patients improved in the functional and echocardiographic tests. Patients who did not benefit from the CRT showed a significant increase in the sIL-6R concentration. The analysis of sCD163 and sTWEAK levels showed that patients with HF-REF are characterized by a lower concentration sTWEAK in comparison with comorbidities-matched controls. In contrast, they had higher concentrations of sTWEAK, sCD163 as well as the sTWEAK / sCD163 ratio compared to healthy volunteers.

The study showed that HF-REF patients present the limited exercise tolerance and impaired exercise ventilation compared to those without the CHF history. CRT is associated with the improvement in some of these parameters. HF-REF is associated with changes in the IL-6 and sIL-6R levels, but the CRT-related improvement in patients' clinical status does not significantly influence their concentrations, while patients who did not benefit from CRT presented an increase in the sIL-6R concentration. This fact suggests a relationship of the unsatisfactory CRT response with the higher IL-6 activity related to the transsignaling. The sTWEAK and sCD163 analysis showed higher concentrations of these mediators in HF-REF patients compared to healthy volunteers, while the effect of heart failure when compared to comorbidities-matched cohort seems to be associated with the sTWEAK decrease. Moreover, the relatively higher sTWEAK to sCD163 ratio suggests that the activity of sTWEAK may be increased in the course of cardiovascular diseases. These results indicate the need for further long-term studies in order to get the better knowledge of the exact role of the inflammatory mediators in chronic heart failure.