THE ROLE OF INTRACELLULAR IRON IN LYMFO/MONOCYTES IN ATHEROGENETIC PROCESS

MUDr. Peter Riško

Background:

The increased storage iron level is connected to a higher frequency of cardiovascular events (CVE).

Aims and hypothesis:

The study investigates the relationship between LIP (labile iron pool) in circulating monocytes and markers of iron metabolism and atherosclerosis (inflammation, oxidative stress, endothelial dysfunction and arterial elasticity) in patients with chronic cardiovascular disease and in healthy volunteers and in long-term blood donors and healthy non-donor volunteers.

Methods:

A detailed medical history was obtained from the probands and anthropometric measurements (body height, weight and waist, calculation of body mass index and waist-hip ratio) were performed. The following parameters were measured / calculated for all respondents: blood pressure (systolic / diastolic), ankle-brachial index (ABI), pulse pressure and mean arterial pressure, cardio-ankle vascular index (CAVI), augmentation index (AI), pre-ejection time (PEP) and ejection time (ET), sonographic examination of abdomen and carotid arteries were performed. Blood samples were collected in the morning after at least 10 hours of fasting. We performed a basic biochemical examination and measured the parameters of inflammation, endothelial dysfunction, oxidative stress. We measured LIP levels in isolated monocytes.

Results:

The patients with a history of CVEs had significantly higher LIP values than did the control group (1.94±0.46 μM vs. 1.62±0.49 μM, p=0.02). Except for the leukocyte number, the groups did not differ in other inflammatory markers (CRPus, CD 163, MPO, MMP-1). Similarly, there were no differences in the markers of endothelial dysfunction (ICAM, VCAM, E-selectin, vWF). The CVE group had higher pulse pressures, levels of markers of impaired arterial elasticity (AI, Young´s modulus, pulsatility, stiffness index), IMT values and ABI values. The LIP concentration was significantly correlated with the transferrin receptor⁄ferritin ratio, hepcidin levels, visceral fat tissue content and the ABI and ET (ejection time) values. Further analysis showed that the OR for acute CVE was 6 fold higher when LIP tertiles were compared (OR=5.96, P=0.0156).

We found that donors had significantly higher LIP values than the control group (1.84 ± 0.44 uM vs. 1.50 ± 0.41 uM, p = 0.017). Despite the observed tendency for the donor group to have higher blood pressure, cholesterol, glucose and HOMAR-IR, the groups did not differ in inflammatory markers, markers of endothelial dysfunction and markers of impaired arterial elasticity. The donor group had significant changes in iron metabolism (higher serum Fe, ceruloplasmin, and transferrin receptor/ferritin ratio and lower hepcidin, ferritin, and CD163), indicating depletion of body iron stores and activation of iron turnover.

Conclusions:

Patients with a history of CVE have significantly higher concentrations of intracellular LIP in circulating monocytes than do healthy controls. The independent and significant correlation of LIP with markers of the progression of atherosclerosis and arterial stiffness suggests LIP as a possible marker of atherosclerotic activity in patients with chronic cardiovascular disease.

LIP seems to be a good marker of iron turnover activity in donor group. We did not find a significant correlation between LIP levels and atherosclerosis progression between donor and non-donor group. However, further studies are needed to assess long-term donorship as a protective factor against atherosclerosis.