The metabolic response to acute coronary syndrome focusing on tissue factor,, metalloproteinases and soluble CD40 ligand

Introduction:

The cause of acute coronary syndrome is unstable plaque and its rupture. Pathogenesis is complex and requires various mechanisms and depends both on the composition of plaque and thrombotic activity of blood.

Objectives:

The main goal of this work was to assess local levels of plasma tissue factor (TF), tissue factor inhibitor (TFPI), tissue metalloproteinases (MMP-2, 3 and 9) and inhibitor of metalloproteinases-2 (TIMP-2), a highly selective C-reactive protein (CRP) and soluble CD40 ligand (sCD40L) in patients with acute coronary syndrome and with stable angina pectoris in the systemic circulation, the coronary sinus and to determine the time course of blood levels in patients with acute coronary syndrome.

Methods and results:

Study population include patients with coronary artery disease (CAD). In 24 patients with stable CAD (SCAD) at time of diagnostic coronary angiography, we withdrew samples from the coronary sinus (CS), femoral vein (VF) and left coronary artery (LMCA). In 29 patients with acute coronary syndrome (ACS) we took samples of venous blood also 24 hours and 7 days from the start. The samples were fixed levels of TF, TFPI, MMP-2, 3 and 9, TIMP-2, CRP, and sCD40L.

Plasma tissue factor levels were significantly higher in patients with acute coronary syndrome than in patients with stable coronary heart disease (239,0±99,3 pg/ml vs. 164,3±114,2 pg/ml, p = 0,016). Levels in the ACS group had a statistically insignificant trend toward decrease on day 7. Levels of MMP-9 were significantly higher in patients with ACS than SCAD (815,5±451,8 mg/l vs. 504,8±245,7 mg/l, p = 0,004). Levels of sCD40L were higher in CS in ACS group than in SCAD patients (9070,5± 4539,3 pg/ml vs. 6841,4 ± 3283,8 pg/ml; p=0,026). Transcoronary gradient - the difference of sCD40L levels between LMCA and CS was significantly higher in patients with ACS (p=0,041). hsCRP levels were significantly increased in the ACS group (14,7±20,9 ng/ml vs. 3,99±7,05 ng/ml, p=0,013) with the trend on insignificant rise 24 h (20,9±26,6 ng/ml) and the seventh day (24.4±42,7 ng/ml). The levels of TFPI, MMP-2, MMP-3 and TIMP-2 did not differ statistically between groups.

There is a moderate positive correlation between the levels of tissue factor and highly sensitive CRP (r=0.34, p=0.016). We found moderately strong positive correlation between the levels of tissue factor and the level of soluble CD40 ligand (r=0.49, p<0.005), and between the levels of metalloproteinase 9 and highly sensitive CRP levels were found moderate positive correlation (r=0.32, p=0.02).

Conclusions:

We confirmed the important role of tissue factor in the physiology and pathophysiology of acute coronary syndrome, TF can serve as a potential target to influence the thrombotic process at the beginning of the coagulation cascade. Levels of sCD40 are related to platelet activity, transcoronary gradient indicates a significant increase of activity thrombocytes and demonstrates the need for sufficient blockade of thrombocytes in acute coronary syndrome. Levels of TF, sCD40 and CRP correlate and relate with atherothrombotic activity. Correlation of MMP-9 and CRP may connect inflammatory and thrombotic process.