Abstract

The poor platelet responsiveness to antiplatelet treatment with acetylsalicylic acid (aspirin, ASA) in some subpopulation of patients, including those with coronary artery disease, can be induced by multiple factors. Not all of them have been recognized to date.

In a cross-over randomized controlled intervention multicenter study we evaluated blood platelet response to ASA administered daily for 30 days at a dose of 75 or 150 mg/day to patients with coronary artery disease. Using three-parametric analysis (the comprehensive score), including the results of whole blood impedance platelet aggregometry stimulated with either arachidonic acid or collagen and the results of *in vitro* dynamic generation of thromboxane B_2 in a whole blood, we evaluated platelet "aspirin-sensitivity" in relation to blood morphological and biochemical parameters.

We have shown that beside biochemical parameters, like markers of dyslipidaemia and glycaemic control, homocysteine, the non-protein, thiol amino acid, exhibits the strongest association with comprehensive scores of platelet "aspirin-resistance". Importantly, the increase of daily ASA dose from 75 to 150 mg overcomes poor platelet responsiveness to ASA treatment, despite the still existing hyperhomocysteinaemia.

In an *in vitro* study preliminary results have been obtained, suggesting that overcoming of homocysteine-associated platelet "aspirin-resistance" may be a result of the generation of N-acetylhomocysteine, acting as antiplatelet factor, contrary to its parental, non-acetylated precursor.

Additionally, we have shown the importance of blood haematocrit as the second of newly recognized factors contributing to a generation of blood platelet "aspirin-resistance".

In the case of haematocrit, similarly to hyperhomocysteinaemia, doubling of daily acetylsalicylic acid dose resulted in a reduced platelet "aspirin-resistance" and in the increased platelet sensitivity to the treatment with acetylsalicylic acid.