Vitamin D levels and Tissue Factor expression in acute coronary syndrome patients

1)Brambilla M. 2)De metrio M. 3)Canzano P. 4)Rossetti L. 5)Cosentino N. 6)Tremoli E. 7)Marenzi GC. 8)Camera M.

Centro Cardiologico Monzino

Introduction. Clinical and epidemiologic studies have revealed an association between vitamin D (Vit D) deficiency and increased risk of cardiovascular diseases. Platelets play a major role in cardiovascular events and lower Vit D levels have been associated with higher platelet reactivity and impaired effectiveness of pharmacological treatment with ADP-antagonists. The antithrombotic effect of Vit D may also be related to its capacity to down-regulate tissue factor (TF), the main activator of blood coagulation, which is expressed also by platelets.

Aim. The aim of this study was to evaluate the relationship between Vit D levels and platelet Tissue Factor expression in non-ST elevation myocardial infarction (NSTEMI) patients.

Methods. Sixtyeight NSTEMI patients were enrolled: 38 subjects were on double antiplatelet therapy –DAT- and 30 were on aspirin only. Platelet surface TF expression and platelet activation markers (P-selectin and phosphatidilserine (PS) membrane exposure by Annexin V binding) were assessed by whole blood flow cytometry, in resting conditions and upon ADP stimulation. Vit D serum levels were measured with Architect 25-OH vitamin D assay. The global haemostatic potential of whole blood was evaluated by thromboelastometry (ROTEM).

Results. In DAT patients, the levels of platelet activation markers were significantly associated with Vit D levels. Indeed, serum levels of Vit D were inversely correlated with the number of platelets expressing P-selectin (r=-0,54, p=0.001), exposing PS (r=-0,43, p=0.018) and with the number of TF-positive platelets both under resting condition (r=-0.43, p=0.024) and after ADP activation (r=-0,55, p=0.002). In particular, patients with Vit D levels lower than the median value of the whole group (17 ng/ml) had a 2-fold higher number of TF-positive platelets, upon ADP stimulation, compared to patients with higher Vit D levels (p=0.005). Of interest, the percentage of TF-positive platelets of DAT patients with low Vit D levels was comparable to that measured in patients treated with aspirin only, suggesting a higher platelet reactivity despite the double antiplatelet therapy. Analysis of the global haemostatic potential showed that patients with low levels of Vit D had a faster clotting kinetics (CT: 435±169 vs 793±215, p=0,03; CFT : 112±34 vs 207±43, p=0,007, respectively) and formed a larger clot (MCF:63±6 vs 55±5, p=0,01, respectively) compared to patients with higher Vit D levels.

Conclusions. These data indicate that lower Vit D levels are associated with a higher platelet reactivity. In particular, the number of circulating platelets that express TF are increased in NSTEMI patients with low levels of Vit D, thus being able to support the higher prothrombotic potential measured in these patients. These evidences highlight the association between acute coronary syndrome and Vit D deficiency, opening challenging for future studies on the possible role of Vit D supplementation in improving cardiovascular outcome.