



PLATELET HYPERREACTIVITY AND PROCOAGULANT PHENOTYPE IN ESSENTIAL THROMBOCYTHEMIA: INSIGHTS FROM ADVANCED PLATELET FUNCTION TESTING

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Backgrounds and aims. Essential thrombocythemia (ET) is a myeloproliferative neoplasm (MPN) that increases the risk of vascular events. Enhanced platelet activation is involved in pathogenesis of thrombosis in ET and the hallmark of thrombotic prevention is the use of the antiplatelet agent aspirin. Aim of the study was to identify platelet phenotype and innovative applicable laboratory approaches to improve risk scores and eventually prognostic value in ET patients.

Methods. In blood samples from patients with TE (n=40,15M, age:65±16 years) and healthy volunteers (n=47,18M, age:45±18 years) we assessed: i) percent maximal aggregation (MA) in platelet-rich plasma in response to agonists; ii) the activation of α IIB β 3 (defined as % platelets positive to PAC1 antibody binding); iii) thrombogenicity of whole blood using the Thrombosis Formation Analysis System (T-TAS) which measures platelet thrombus formation (PL chip) or fibrin formation (AR chip) mimicking the coagulation process under shear forces, both expressed as area under curve (AUC). Informed consent was obtained and the study was approved by Territorial Ethics Committee.

Results. ET patients, if compared to healthy subjects, showed increased aggregability, specifically to ADP (2.5 μ M)

(63±7 vs 40±5, p=0.016) and thrombin receptor-activating peptide-6 (TRAP-6, 5 μ M) (44±8 vs 6±2, p=0.016). About 20% of on aspirin patients showed MA to arachidonic acid (1mmol/l) higher than 20%, thus indicating an incomplete effect of aspirin. If compared to healthy subjects (0.50±0.07) a decrease of PAC-1 binding was evident in platelets from ET patients both in the absence (0.16±0.03, p<0.001) and presence (0.31±0.03, p=0.04) of aspirin treatment. AUC values of PL T-TAS positively correlated with aggregations to 2.5 μ M ADP (r=0.524, p=0.015), 4mg/L collagen (r=0.517, p=0.016), and 5 μ M epinephrine (r=0.395, p=0.017) whereas AUC values of AR T-TAS inversely correlated with PAC-1 expression (r=0.664, p=0.018).

Conclusions. Collectively, these results indicate that platelets from ET patients show increased activation and aggregability even when exposed to aspirin. Furthermore, the reduced expression of active α IIB β 3a in a significant subset of platelets likely mirrors their procoagulant phenotype. Because ET management relies on risk stratification, our data also suggest that T-TAS could represent a reliable screening test for platelet function and coagulation by helping to identify the hypercoagulable state in ET.