Thromboxane pathway and venous thrombosis: ASA effects in mouse model

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Background: Data from several trials suggest tat acetylsalicylic acid (Aspirin or ASA) reduces the incidence of venous thromboembolism in human. However, information available on the mechanisms involved in this effect are limited.
Aim: The aim of this study was to assess the effects of ASA in venous thrombosis and to explain the possible molecular mechanisms at the base of this effect using a mouse model.
Methods: For in vivo experiments, wild type (WT) mice were randomized in three groups: control group (treated with vehicle), ASA group (treated with ASA 30 mg/Kg gavage), and the last SQ 29,548 group (treated with a selective thromboxane receptor antagonist 2 mg/kg i.p.). After treatment, mice were subjected to ligation of the inferior vena cava (IVC) to induce venous thrombosis. Urines of control and ASA groups were collected during the experiments to measure 2,3-dinor Thromboxane B2 (TXB-M) levels. At sacrifice of animals, 48 hours after IVC ligation, thrombi and blood were collected for subsequent analysis. In vitro experiments were performed on mouse peritoneal macrophages incubated with different compounds.
Results: In control mice, 24 hours after IVC ligation, TXB-M levels in urine were significantly higher than at baseline, and they decreased slightly after 48 hours. Administration of ASA was associated with significant reduction of TXB-M in urine at 24 and 48 hours compared to control mice. Moreover, ASA treatment significantly decreased the mass of thrombi characterized by lower amounts of Tissue Factor (TF) expression. Also, TF activity in plasma of ASA group was decreased compare to control. A positive correlation between the size of thrombi and TXB-M urinary concentration, as well as between TXB-M and plasma TF activity was observed. To confirm a possible involvement of thromboxane pathway in this contest, treatment with SQ 29,548 was performed. SQ 29,548 caused significantly reduction of thrombus weight compare to control group, associated to a significantly reduction also in TF expression.
In vitro study showed that TF activity of mouse peritoneal macrophages incubated with supernatants of activated platelets (sPLTs) or with IBOP, a stable TXB2 analogue, was greater than that of control cells. SQ 29,548 treatment completely antagonized this effect.
Conclusion: Our study suggests that ASA treatment, inducing the inhibition of thromboxane pathway, significantly reduce Tissue Factor expression/activity, with consequent decrease of venous thrombus formation. This newly described effect of ASA provides a potential link between platelet activation and the occurrence of venous thrombosis.