TICAGRELOREDUCES NEUTROPHIL RECRUITMENT AND LUNG DAMAGE IN ABDOMINAL SEPSIS

Authors: Oscar Braun, Milladur Rahman, David Gustafsson, Henrik Thorlacius, Skane University Hospital, Lund, Sweden

Background: Platelets play an important role in abdominal sepsis by releasing CD40L in the circulation, which subsequently activates neutrophils and promotes pulmonary infiltration of neutrophils and tissue damage. Platelet depletion has been shown to substantially decrease lung damage and neutrophil infiltration in abdominal sepsis in mice. Herein, we assessed the impact of platelet inhibition with ticagrelor on pulmonary neutrophil recruitment and lung damage in a mouse model of abdominal sepsis.

Methods: Wild-type C57BL/6 mice were subjected to cecal ligation and puncture (CLP). Animals were pretreated with ticagrelor (100 mg/kg) or vehicle prior to CLP induction. Edema formation, myeloperoxidase (MPO) levels and bronchoalveolar neutrophils in the lung as well as plasma levels of CD40L were quantified. Flow cytometry was used to determine expression of platelet-neutrophil aggregates and CD40L on platelets.

Results: MPO levels in the lung 6 hours after CLP-induction were not affected by ticagrelor. After 24 hours’ treatment with ticagrelor there was reduced sepsis-induced pulmonary infiltration of neutrophils by 50% (P < 0.05 vs. sham, n = 6), lung edema (wet/dry ratio was reduced from 4.99 ± 0.04 to 4.51 ± 0.07, P < 0.05 vs. sham, n = 6), and lung damage (lung damage score was reduced by 41%, P < 0.05 vs. sham, n = 6). Ticagrelor also prevented formation of platelet-neutrophil aggregates and sepsis-induced thrombocytopenia. Ticagrelor reduced sepsis-induced decreases of platelet-bound CD40L, but the soluble levels of CD40L were not affected by the treatment.

Conclusions: Our data indicate that ticagrelor can reduce pulmonary neutrophil recruitment and lung damage in abdominal sepsis, suggesting a potential role for platelet inhibition in treating or perhaps preventing the tissue damage associated with sepsis.