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MEETING ABSTRACT

A1.1

Potent irreversible $P2Y_{12}$ inhibition does not reduce LPS-induced coagulation activation in a randomized, double-blind, placebo-controlled trial

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Background: Platelets play an important role in coagulation activation. $P2Y_{12}$ receptor inhibition may be beneficial in inflammatory states. Prasugrel, a potent, irreversible inhibitor of $P2Y_{12}$ receptor-induced platelet activation may reduce coagulation activation in a human LPS model.
Methods: A double-blind, randomized, crossover trial with a minimum washout period of 6 weeks was performed. Sixteen subjects were randomly assigned to a treatment group that received prasugrel or placebo two hours prior to infusion of a bolus of LPS (2 ng/kg body weight), while four subjects were assigned to a control group receiving prasugrel or placebo without LPS. Histone-complexed DNA (hcDNA), coagulation- and platelet-specific parameters were measured by enzyme immunoassay. Leukocyte aggregate formation was analyzed by flow cytometry, and thromboelastometry was performed.
Results: LPS infusion markedly activated coagulation. However, prasugrel did not reduce changes in prothrombin fragment F1+2, thrombin–antithrombin complexes, microparticle-associated tissue factor, CD40 ligand, P-selectin, platelet–leukocyte aggregation, hcDNA levels or the coagulation profile measured by thromboelastometry. hcDNA plasma levels increased approximately six-fold after LPS infusion in both treatment groups, but not in the control groups.
Discussion: Potent irreversible $P2Y_{12}$ inhibition by prasugrel does not affect LPS-induced coagulation activation. hcDNA plasma levels increased six-fold after infusion of LPS, indicating the formation of neutrophil extracellular traps during sterile inflammation.

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