Human plasma thrombopoietin levels are regulated by binding to platelet thrombopoietin receptors in vivo

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BACKGROUND: Data from several studies support the hypothesis that thrombopoietin (TPO) plasma levels are regulated via circulating platelet (PLT) numbers by binding to PLT TPO receptors (TPO-Rs). In this study, PLT numbers and TPO plasma levels were measured following the transfusion of unmanipulated, sham-saturated, and TPO-R-saturated PLT preparations to provide additional in vivo evidence for this regulatory mechanism. STUDY DESIGN AND METHODS: Following in vitro experiments to characterize pegylated recombinant human megakaryocyte growth and development factor (PEG-rHuMGDF) binding characteristics, PLT numbers and TPO plasma levels were measured following the transfusion of unmanipulated, sham-saturated, and TPO-R-saturated PLT preparations in thrombocytopenic patients. Sham-saturated and TPO-R-saturated PLTs were prepared by a 1-hour incubation without and with 40 ng per mL of PEG-rHuMGDF, respectively, and subsequent washing and resuspension. RESULTS: In vitro, 2.72 +/- 0.8 ng of PEG-rHuMGDF per 1 x 10^8 PLTs was bound within 1 hour of incubation. No additional PEG-rHuMGDF was bound following a second incubation with PEG-rHuMGDF, and bound PEG-rHuMGDF was not released over time. In vivo, TPO plasma levels decreased significantly (p < 0.001), by 30.7 +/- 5.8 and 20.9 +/- 2.1 percent after transfusion of unmanipulated and sham-saturated PLT preparations, respectively. However, TPO plasma levels were unaffected after the transfusion of TPO-R-saturated PLTs despite comparable transfusion-induced PLT count increases. CONCLUSION: These data strongly support the concept that binding to PLT TPO-R is directly involved in human TPO plasma level regulation in vivo.

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