Reduction in lipopolysaccharide-induced thrombocytopenial by triflavin in a rat model of septicemia

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摘要

Abstract

BACKGROUND: Thrombocytopenia frequently occurs early in the course of Gram-negative bacterial infections. Triflavin, an Arg-Gly-Asp-containing disintegrin, has been suggested to interfere with the interaction of fibrinogen with the glycoprotein IIb/IIIa complex. The present study was undertaken to determine whether triflavin could prevent thrombocytopenia in lipopolysaccharide (LPS)-treated rats. METHODS AND RESULTS: In this study, 51Cr-labeled platelets were used to assess blood and tissue platelet accumulation after LPS challenge. The administration of LPS (4 mg/kg IV bolus) for 4 hours induced a reduction in radiolabeled platelets in blood and an obvious accumulation of platelets in liver. Triflavin (500 microg/kg) but not GRGDS (20 mg/kg) significantly prevented the alteration of radiolabeled platelet distribution in blood and liver when induced by LPS. Furthermore, triflavin but not GRGDS markedly suppressed the elevation in plasma thromboxane B2 concentration within the 4-hour period of LPS administration. In LPS-treated rats, the 5-hydroxytryptamine level was lower in the blood and higher in the liver compared with levels in normal saline-treated rats. Pretreatment with triflavin (500 microg/kg) significantly reversed the 5-hydroxytryptamine concentration in blood and liver of LPS-treated rats. In histological examinations and platelet adhesion assay, triflavin markedly inhibited the adhesion of platelets to subendothelial matrixes in vivo and in vitro. CONCLUSIONS: The results indicate that triflavin effectively prevents thrombocytopenia, possibly through the following 2 mechanisms: (1) Triflavin markedly inhibits platelet aggregation, resulting in decreased thromboxane A2 formation. (2) It inhibits the adhesion of platelets to subendothelial matrixes, thereby leading to a reversal in the distribution of platelets in blood and liver in LPS-treated rats