Mechanism Involved in the Antiplatelet Activity of Staphylococcus aureus Lipoteichoic Acid in Human Platelet

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摘要

Abstract

In this study, gram-positive Staphylococcus aureus lipoteichoic acid (LTA) dose-dependently (0.1-1.0 microg/ml) and time-dependently (10-60 min) inhibited platelet aggregation in human platelets stimulated by agonists. LTA also dose-dependently inhibited phosphoinositide breakdown and intracellular Ca+2 mobilization in human platelets stimulated by collagen. LTA (0.5 and 1.0 microg/ml) also significantly inhibited thromboxane A2 formation stimulated by collagen in human platelets. Moreover, LTA (0.1-1.0 microg/ml) dose-dependently decreased the fluorescence of platelet membranes tagged with diphenylhexatrience. Rapid phosphorylation of a platelet protein of Mr. 47,000 (P47), a marker of protein kinase C activation, was triggered by PDBu (30 nM). This phosphorylation was markedly inhibited by LTA (0.5 and 1.0 microg/ml) within a 10-min incubation period. These results indicate that the antiplatelet activity of LTA may be involved in the following pathways: LTA's effects may initially be due to induction of conformational changes in the platelet membrane, leading to a change in the activity of phospholipase C, and subsequent inhibition of phosphoinositide breakdown and thromboxane A2 formation, thereby leading to inhibition of both intracellular Ca+2 mobilization and phosphorylation of P47 protein. Therefore, LTA-mediated alteration of platelet function may contribute to bleeding diathesis in gram-positive septicemic and endotoxemic patients.