

Low concentration of oxidized low density lipoprotein suppresses platelet reactivity in vitro: an intracellular study

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摘要

Abstract

The intracellular mechanisms underlying oxidized low density lipoprotein (oxLDL)-signaling pathways in platelets remain obscure and findings have been controversial. Therefore, we examined the influence of oxLDL in washed human platelets. In this study, oxLDL concentration-dependently (20-100 microg/mL) inhibited platelet aggregation in human platelets stimulated by collagen (1 microg/mL) and arachidonic acid (60 microM), but not by thrombin (0.02 U/mL). The activity of oxLDL was greater at 24 h in inhibiting platelet aggregation than at 12 h. At 24 h, oxLDL concentration-dependently inhibited intracellular Ca²⁺ mobilization and thromboxane B₂ formation in human platelets stimulated by collagen. In addition, at 24 h oxLDL (40 and 80 microg/mL) significantly increased the formation of cyclic AMP, but not cyclic GMP or nitrate. In an ESR study, 24 h-oxLDL (40 microg/mL) markedly reduced the ESR signal intensity of hydroxyl radicals (OH⁻) in both collagen (2 microg/mL)-activated platelets and Fenton reaction (H₂O₂ + Fe²⁺). The inhibitory effect of oxLDL may induce radical-radical termination reactions by oxLDL-derived lipid radical interactions with free radicals (such as hydroxyl radicals) released from activated platelets, with a resultant lowering of intracellular Ca²⁺ mobilization, followed by inhibition of thromboxane A₂ formation, thereby leading to increased cyclic AMP formation and finally inhibited platelet aggregation. This study provides new insights concerning the effect of oxLDL in platelet aggregation.