Mechanisms involved in the antiplatelet activity of ketamine in human platelets

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摘要

Abstract

The aim of this study was to systematically examine the inhibitory mechanisms of ketamine in platelet aggregation. In this study, ketamine concentration-dependently (100-350 microM) inhibited platelet aggregation both in washed human platelet suspensions and platelet-rich plasma stimulated by agonists. Ketamine inhibited phosphoinositide breakdown and intracellular Ca2+ mobilization in human platelets stimulated by collagen. Ketamine (200 and 350 microM) significantly inhibited thromboxane (Tx) A2 formation stimulated by collagen. Moreover, ketamine (200 and 350 microM) increased the fluorescence of platelet membranes tagged with diphenylhexatriene. Rapid phosphorylation of a platelet protein of Mr 47,000 (P47), a marker of protein kinase C activation, was triggered by phorbol-12,13-dibutyrate (100 nM). This phosphorylation was markedly inhibited by ketamine (350 microM). These results indicate that the antiplatelet activity of ketamine may be involved in the following pathways. Ketamine may change platelet membrane fluidity, with a resultant influence on activation of phospholipase C, and subsequent inhibition of phosphoinositide breakdown and phosphorylation of P47, thereby leading to inhibition of intracellular Ca2+ mobilization and TxA2 formation, ultimately resulting in inhibition of platelet aggregation. 2004 National Science Council, ROC and S. Karger AG, Basel