Morphine-potentiated agonist-induced platelet aggregation through a-2 adrenoceptors in human platelet

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摘要

Abstract

Morphine dose-dependently (0.6, 1, and 5 microM) potentiated platelet aggregation and ATP release stimulated by agonists (i.e., collagen and U46619) in washed human platelets. Furthermore, morphine (1 and 5 microM) markedly potentiated collagen (1 microg/ml) evoked an increase of intracellular Ca2+ mobilization in fura 2-AM loading human platelets. Morphine (1 and 5 microM) did not influence the binding of fluorescein isothiocyanate-triflavin to platelet glycoprotein IIb/IIIa complex. Yohimbine (0.1 microM), a specific alpha2-adrenoceptor antagonist, markedly abolished the potentiation of morphine in platelet aggregation stimulated by collagen. Moreover, morphine (0.6-5 microM) markedly inhibited prostaglandin E1 (10 microM)-induced cAMP formation in human platelets, and yohimbine (0.1 microM) significantly reversed the inhibition of cAMP by morphine (0.6 and 1 microM) in this study. Morphine (1 and 5 microM) significantly potentiated thromboxane B2 formation stimulated by collagen in human platelets, and yohimbine also reversed this effect of morphine in this study. In addition, morphine (1 and 5 microM) did not significantly affect nitrate production in human platelets. Morphine may exert its potentiation in platelet aggregation by binding to alpha2-adrenoceptors in human platelets, which leads to reduced cAMP formation and subsequently to increased intracellular Ca2+ mobilization; this, in turn, is followed by increased thromboxane A formation and finally potentiates platelet aggregation and ATP release.