

Mechanisms involved in agonist-induced hyperaggregability of platelets from normal pregnancy

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摘要

Abstract

There is substantial evidence of increased platelet reactivity in vivo and in vitro during pregnancy. Platelet activation occurs in pregnancy with a risk of the development of preeclampsia. In this study, platelet behavior was studied during 28 – 40 weeks of gestation in a group of women who remained normotensive and a group of nonpregnant female controls. Platelet aggregation and ATP release stimulated by agonists (i.e. collagen and adenosine 5-diphosphate) were markedly enhanced in washed platelets from pregnant subjects. Furthermore, the collagen-evoked increase in intracellular Ca^{2+} ($[Ca^{2+}]_i$) mobilization in fura-2-AM-loaded platelets was also enhanced in pregnant subjects. Moreover, the binding activity of fluorescein isothiocyanate-triflavin toward the platelet glycoprotein IIb/IIIa complex did not significantly differ between the nonpregnant and pregnant groups. In addition, the amount of thromboxane A₂ (TxA₂) formation from pregnant subjects was significantly greater than that from nonpregnant subjects in both resting and collagen-activated platelets. On the other hand, prostaglandin E₂ formation in the presence of imidazole in either resting or arachidonic acid (100 μ M)-treated platelets did not significantly differ between these two groups. The levels of cyclic AMP formation in both resting and prostaglandin E₁ (10 μ M)-treated platelets from pregnant subjects were significantly lower than those in nonpregnant subjects. Nitric oxide production was measured by a chemiluminescence detection method in this study. The extent of nitrate production in either resting or collagen-stimulated platelets from pregnant subjects did not significantly differ from that of platelets from the nonpregnant group. We conclude that the agonist-induced hyperaggregability of platelets from normal pregnancy may be due, at least partly, to an increase in TxA₂ formation and a lowering of the level of cyclic AMP formation, which leads to increased $[Ca^{2+}]_i$ mobilization and finally to enhanced platelet aggregation and ATP release.