Potentiating effect of prostaglandin $F_{2\alpha}$ on platelet aggregation in mice

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Background: Platelets play an important role in both physiological hemostasis and pathological thrombosis. Among prostanoids, consisting of prostaglandins (PGs) and thromboxane (TX), TXA_2 and PGI_2 are well known as a potent stimulator and an inhibitor of platelets, respectively. Recently, PGE_2 has also been reported to regulate platelet function via the PGE_2 receptor subtypes. However, the effect of $PGF_{2\alpha}$ on platelet function remains to be determined. Here we examined the effect of $PGF_{2\alpha}$ on platelet aggregation.

Methods: We used male mice lacking the prostanoid receptor: $PGF_{2\alpha}$ receptor FP, PGE_2 receptor subtype EP_3 , TXA_2 receptor TP and both EP_3 and TP. Wild-type (WT) mice were used as a control of these mice. We prepared platelets from these mice and assessed platelet aggregation by light transmission aggregometry. In vivo, we measured bleeding time to examine the effect of $PGF_{2\alpha}$ on hemostasis. Moreover, the effect of $PGF_{2\alpha}$ on thrombosis was evaluated in an arachidonic acid-induced acute thromboembolism model.

Results: In WT platelets, $PGF_{2\alpha}$ potentiated adenosine diphosphate (ADP)-induced aggregation in a concentration-dependent manner, while $PGF_{2\alpha}$ alone did not induce aggregation. In platelets lacking FP, however, the potentiating effect of $PGF_{2\alpha}$ on ADP-induced aggregation was not significantly different from that in WT platelets. Interestingly, the potentiating action of $PGF_{2\alpha}$ was significantly blunted in platelets lacking EP_3 or TP, and completely disappeared in platelets lacking both EP_3 and TP. Intravenously administered $PGF_{2\alpha}$ significantly shortened the bleeding time and increased mortality in an arachidonic acid-induced acute thromboembolism model in WT mice, suggesting that $PGF_{2\alpha}$ acts as a platelet stimulator also in vivo.

Conclusions: $PGF_{2\alpha}$ potentiates platelet aggregation via EP_3 and TP, but not via FP. Accordingly, $PGF_{2\alpha}$ is involved in hemostasis and thrombosis in mice.