

Platelet activity, coagulation, and fibrinolysis during exercise in healthy males: effects of thrombin inhibition by argatroban and enoxaparin.

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BACKGROUND: Relationships between exercise-induced activation of platelets, blood coagulation, and fibrinolysis, and the importance of thrombin for responses to exercise are not clear. **METHODS AND RESULTS:** Effects of thrombin inhibition on hemostatic parameters were examined in a double-blind crossover study comparing the direct thrombin inhibitor argatroban (350 microg/kg intravenous bolus followed by 25 microg/kg per minute of infusion), the indirect thrombin inhibitor enoxaparin (0.75 mg/kg, intravenous bolus), or placebo (saline) in 21 healthy males. Measurements were made at rest, before and during/after thrombin inhibitor treatment, and immediately after exhaustive exercise. At rest argatroban abolished, and enoxaparin attenuated platelet activation by thrombin, but not by adenosine diphosphate. Argatroban and, even more so, enoxaparin decreased thrombin generation (prothrombin F1+2) and the coagulation potential, and increased the fibrinolytic potential. Exercise increased circulating activated platelets (from 5.5 ± 0.3 to $9.4 \pm 0.9 \times 10^9/L$; $P < 0.001$), circulating platelet-platelet microaggregates, the platelet responsiveness to in vitro stimulation, leukocyte activation (leukocyte CD11b expression and plasma elastase), and platelet-leukocyte aggregation ($P < 0.01$ for all). Exercise increased coagulation (F1+2; $P < 0.01$) and fibrinolysis, but did not alter the balance between them; fibrin gel permeability increased ($P < 0.01$), probably because of release of endogenous tissue plasminogen activator from the vessel wall. Neither argatroban nor enoxaparin counteracted exercise-induced platelet or leukocyte activation. Both thrombin inhibitors augmented exercise effects on fibrinolysis. **CONCLUSIONS:** Strenuous exercise enhances platelet and leukocyte activation independently of thrombin. Exercise augments both coagulation and fibrinolysis, but the balance between them appears to be maintained. At therapeutic dosages argatroban counteracted thrombin-induced platelet activation most efficiently, whereas enoxaparin had somewhat stronger anticoagulant and profibrinolytic effects.