A COMPARISON BETWEEN FIBRINOLYSIS OF FRESH AND AGED CLOTS OR THROMBI BY rt-PA IN VIVO, EX VIVO AND IN VITRO J. Paul, J. B. Bussmann, B. H. Muller, W. G. Eichert, Department of Biological Research, K. Kuhl, T., University of Germany

In view of the therapeutic applications of rt-PA, it is of interest to investigate whether there is any difference in the lysis efficiency between fresh and aged thrombi. The efficiency of fibrinolysis by rt-PA was studied in three different ways: in vivo, by measuring the thrombus weight of fresh (1 h) or aged (24 h) thrombus in the carotid artery of rabbits, which had been treated with rt-PA, 0.4 mg/kg, or saline for 1 h. In vitro, by measuring the thrombus weight of fresh (1 h) or aged (24 h) thrombus labelled with $^{153}$I-fibrinogen in vitro in plasma containing rt-PA (1 mg/ml), the thrombus was formed in the jugular vein and the carotid artery of each rabbit. In vitro, by measuring $^{153}$I-release of in vivo fresh (1 h) or aged (24 h) thrombus labelled with $^{153}$I-fibrinogen. In vitro, the clot was formed in thejugular vein and the carotid artery of each rabbit. In vivo, by measuring $^{153}$I-release of fresh (1 h) and aged (6 or 24 h) human native whole blood clots, PPP-clots, PRP-clots and squeezed PPP-clots, which were formed and lysed in vitro with rt-PA (1 mg/ml). In vivo as well as in vivo, rt-PA lysed fresh (1 h) thrombus much better than aged (24 h) thrombus. This difference was more pronounced immediately after the onset of fibrinolysis but decreased with time. However, in vitro relatively little difference was observed in fibrinolysis efficiency between fresh (1 h) and aged (24 h) clots. Fibrinolysis of these clots was decreased (PPP < whole blood > PRP) with increasing clot retraction, which was almost complete within 1 h. This result was confirmed when PPP-clots were "retracted" by simply squeezing them just before lysis. Therefore we conclude that a considerable difference in lysis efficiency between fresh and aged thrombus was only observed in vivo and aged in vivo. This difference was less pronounced with increasing fibrinolysis time.

PLATELET INHIBITION (1)

THE THROMBOPHOBIC PROTEIN 4099 INHIBITS THE ADP-AGGREGATION PATHWAY OF HUMAN PLATELETS BY INTERFERING WITH THE BINDING OF FIBRINOGEN TO THE GLYCOPROTEIN IIb-IIIa COMPLEX. J. Bouloux (1), A. Stilar (2), C. Maffrand (2), J.-P. Maffrand (1) INSERM U.311, Centre de Transfusion Sanguine, Strasbourg, France (1) and Sanofi Recherche, Toulouse, France (2).

The thrombopohobic protein 4099, is a synthetic structural analog of actiplatein. After oral administration in man, it prolongs the bleeding time (IPV) and inhibits ADP-induced platelet aggregation. The aim of the study was to evaluate the effects of oral administration of 4099 on human volunteers for 7 days on primary and secondary haemostasis and platelet aggregation. The study was conducted in 40 healthy volunteers (20 men, 20 women) aged 18-27 years who were selected according to the following criteria: no previous history of platelet disorders, no previous treatment with antiplatelet agents, no history of thromboembolic disease. After a baseline study, the patients were randomized in two groups: 20 patients received 4099 (50 mg per day) for 7 days and 20 patients received 4099 (50 mg per day) for 7 days followed by placebo for 7 days. The platelet aggregation was measured in platelet-rich plasma and in platelet-poor plasma. The platelet aggregation was measured by aggregometry and the aggregation was expressed as the percentage of change from baseline. The results showed that 4099 significantly inhibited ADP-induced platelet aggregation in platelet-rich plasma and in platelet-poor plasma. The inhibition of ADP-induced platelet aggregation was dose-dependent. The inhibition of ADP-induced platelet aggregation was also time-dependent. The inhibition of ADP-induced platelet aggregation was higher in platelet-rich plasma than in platelet-poor plasma. The inhibition of ADP-induced platelet aggregation was more pronounced in platelet-rich plasma than in platelet-poor plasma. The inhibition of ADP-induced platelet aggregation was more pronounced in platelet-rich plasma than in platelet-poor plasma. The inhibition of ADP-induced platelet aggregation was more pronounced in platelet-rich plasma than in platelet-poor plasma. The inhibition of ADP-induced platelet aggregation was more pronounced in platelet-rich plasma than in platelet-poor plasma.

INTERACTIONS BETWEEN PG2 AND INHIBITORS OF PLATELET AGGREGATION THAT ACT THROUGH CAMP. S. J. Gray and S. Heptinstall, Department of Medicine, University Hospital, Nottingham, NG7 2QH, UK.

PG2 has a biphasic effect on platelet aggregation with low concentrations of the prostaglandin potentiating aggregation and high concentrations inhibiting it. In this investigation we studied the interaction of PG2 with agents that inhibit platelet aggregation through an effect on CAMP. The agents chosen to raise the level of CAMP in platelets were: 1) agents which potentiate aggregation and CAMP; 2) agents which inhibit platelet aggregation and CAMP; 3) agents which potentiate aggregation and CAMP; 4) agents which inhibit platelet aggregation and CAMP. The agents chosen to raise the level of CAMP in platelets were: 1) agents which potentiate aggregation and CAMP; 2) agents which inhibit platelet aggregation and CAMP; 3) agents which potentiate aggregation and CAMP; 4) agents which inhibit platelet aggregation and CAMP.

PG2, alone or with other agents, inhibited ADP-induced aggregation at $10^{-6}$ M, but did not reduce CAMP levels at any concentration and increased CAMP levels at concentrations $> 10^{-6}$ M, probably by stimulating AC. PG2 inhibited ADP-induced aggregation at $10^{-6}$ M, but did not reduce CAMP levels at any concentration and increased CAMP levels at concentrations $> 10^{-6}$ M, probably by stimulating AC. PG2 inhibited ADP-induced aggregation at $10^{-6}$ M, but did not reduce CAMP levels at any concentration and increased CAMP levels at concentrations $> 10^{-6}$ M, probably by stimulating AC. PG2 inhibited ADP-induced aggregation at $10^{-6}$ M, but did not reduce CAMP levels at any concentration and increased CAMP levels at concentrations $> 10^{-6}$ M, probably by stimulating AC.

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