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Title : INHIBITION OF MICROAGGREGATION BY APROTININ IN ACD-BLOOD

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Introduction: Pulmonary microembolization following transfusion of banked blood might cause impairment of pulmonary function According to recent studies the respiratory disfunction is less a result of the microembolism than the release of biochemical mediators from the cell aggregates. While platelet aggregation is mainly an enzymatically directed process the addition of an enzyme inhibitor to stored blood should inhibit the release of mediators and so the platelet aggregation. The present trial was initiated in order to test the effect of Aprotinin on these pathophysiological reactions.

Methods. I. Influence of Aprotinin on plated aggregation in stored blood: The studies were carried out on 40 units of ACD-blood stored under standard conditions. 200.000 KIU Aprotinin was added to every second unit immediately after donation. The measurements were carried out at 2-4 days interval for 20 days. The presence of microaggregates in stored blood was measured by the screen filtration pressure method of SWANK. Platelet function was assessed on aggregation induced by Adrenalin, ADP and Collagen as described by BORN. Platelet number was done according to the method of DERLATH.

II. Influence of Aprotinin on the thrombocytic and plasmatic coagulation: The effect of 0-10.000 KIU Aprotinin/ml PRP on the platelet aggregation was measured after themethod of BORN and the platelet adhesiveness according to the method of WRIGHT. The influence of different concentrations of Aprotinin on the plasmatic clotting system was assayed on the basis of the PTT.

III. Aprotinin binding to thrombocytic and plasmatic enzyme systems: The character of Aprotinin binding was tested in various experimental models.

a) Thrombocytic System (PRP). Model 1: The interaction between platelets-aprotinin-plasmin. In two aliquots of 1 ml PRP the effect of 1.200 KIU Aprotinin on Adrenalin induced aggregation was tested with and without the addition of 250 I.U. Streptokinase.

Model 2: The interaction between platelets-aprotinin-erythrocytes. In three aliquots of 1 ml PRP the effect of 1.200 KIU Aprotinin on Adrenalin induced aggregation was measured with and without the addition of 1 ml erythrocytes. Before measurement all the above test systems were incubated at 37°C for 1, 20 and 40 minutes.

b) Plasmatic system (PPP). Model 3: The interaction between plasmatic clotting factors aprotinin-erythrocytes. In two aliquots of 1 ml PPP the effect of 2.400 KIU Aprotinin on the PTT was estimated with and without the addition of 2,5 ml erythrocytes. Before measurement the above test systems were incubated at 37°C for 1, 20 and 40 minutes.

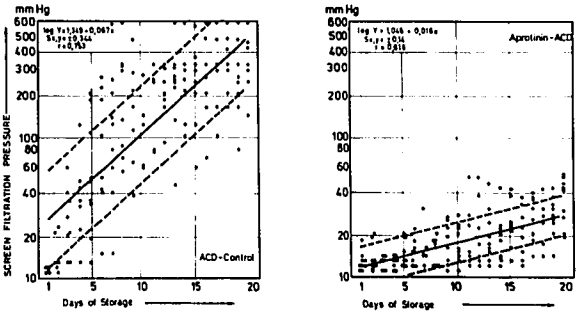
Statistics. The changes in platelet functions were expressed in the form of a regression analysis. The significance of the results was determined by one-way or two-way analysis of variance.

Results. The screen filtration pressure averaged 500 mm Hg after a storage period of 20 days. In contrast, the value for Aprotinin-blood was 30 mm Hg. The aggregation inhibition due to Aprotinin prevented a considerable drop of platelets during storage. Whereas the platelet adhesiveness was not affected by Aprotinin the decrease of collagen and adrenalin-induced aggregation is dependent on the Aprotinin concentration. The binding of Aprotinin was shown to be reversible in both systems. The Aprotinin-platelet complex dissociated in the presence of plasmin or erythrocytes.

Discussion. Aprotinin has a significant inhibiting effect on both the thrombocytic and plasmatic coagulation systems. An inhibitory effect on the inital phase of the plasmatic clotting system was already known. However, the effect on the thrombocytic system could be demonstrated for the first time by using Aprotinin-acd-blood. Aprotinin probably binds to those enzymes that affect membrane permeability so that a release of biochemical mediators that might induce aggregation, are prevented. Furthermore the reversibility of the Aprotinin-binding to the plasmatic and thrombocytic systems was shown Therefore impairments of the haemostasis after transfusion of Aprotinin-acd-blood are not to be expected.

References.

1. Harke H: Prevention of microaggregation in stored blood. Anaesthesist 25: 374-379, 1976



Changes in the screen filtration pressure of ACD- and Aprotinin-ACD-Blood.