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Decreased hematocrit inhibits clotting in rabbits

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Keywords

Cyclic flow reductions, hemodilution

Comments

This study demonstrates that erythrocytes in addition to platelets are required for normal thrombosis. An hematocrit of 23% with a normal platelet count resulted in abolition of the cyclic thrombosis and clot lysis demonstrated by the Foltz model and prolonged the bleeding time. Possible reasons for this are discussed and the paper is well referenced. The results suggest a direct effect on platelet aggregation of a gelatin plasma expander (Plasmion, Rhone Polenc Rorer). The authors make a comment that bleeding time showed a tendancy to be prolonged following re-infusion of shed blood in the gelatin group. This conclusion seems very unlikely from the data in that the differences were non significant and there was a wide spread of data in both groups.These data represent an interesting finding and should prompt further research into the effects of intraoperative hemodilution and the current trend to tolerate lower hemoglobin concentrations in intensive care units.

Introduction

Alterations in hematocrit are known to have effects on hemostasis. Erythrocytes provide agonists for platelet action such as adenosine diphosphate (ADP), facilitate platelet accretion to the endothelium and enhance platelet activity. In rabbit models thrombocytopenia and low hematocrit have been shown to be independent variables which influence haemostasis. Additionally metabolically active erythrocytes have been shown to enhance the platelet release reaction, eicosanoid synthesis and further platelet recruitment. An animal model of arterial thrombosis has been developed (the Foltz model) This involves arterial wall damage and stenosis which induces thrombosis followed by embolisation of the platelet plug leading to cyclical flow reduction (CFR).

Aims

To determine the effects of a decrease in hematocrit with a stable platelet count on thrombosis in the Foltz model and to assess the bleeding time from a ear incision and transected spleen.

Methods

A total of 37 male New Zealand rabbits were anesthetized. Body temperature, blood pressure and heart electrical activity were monitored continuously. The right carotid artery was exposed and blood flow was monitored using an electromagnetic circular flow probe. After 10 min stabilization, the artery was clamped to produce 60% stenosis, and after a further 10 min the clamp was released. Arterial injury was induced (via three rapid consecutive cross-clampings of the artery) and the stenosis reapplied, triggering a series of CFRs (here, a repetitive decrease in blood flow followed by an abrupt return to normal flow) which were monitored for 20 min. This period was defined as CFR1. A further two CFR periods were monitored; CFR2 and CFR3, each preceded by a rest period. Four points of measurement were defined: T0 (start CFR1), T1 (end CFR1), T2 (end CFR2) and T3 (end CFR3). After CFR1 the animals were randomly divided into 3 groups:

1) Control group: no treatment, measurement of CFR2 and 3 followed by wound and spleen bleeding measurements.

2) Platelet-rich plasma (PRP) group: animals hemodiluted with PRP until hematocrit reached 23%, measurement of CFR2 and 3 followed by wound and spleen bleeding measurements.

3) Gelatin solution group: normovolemic hemodilution via infusion of a gelatin solution until hematocrit reached 23%, blood collected, measurement of CFR2. Blood was reinfused (over 20 min) followed by measurement of CFR3 and then wound and spleen bleeding measurements.

At the beginning of the experiment and after each CFR measurement, the ear immersion bleeding time was measured. Blood samples were taken at each of the T-points. Hematocrit levels, platelet counts, prothrombin time, fibrinogen and platelet aggregation measurements were taken. Blood gases were measured at T0 and T2.

Results

Only 24 rabbits could be included in the analysis. The control group showed no variation in hematocrit levels. In the PRP group, hematocrit levels decreased, then stabilized. In the gelatin group, hematocrit decreased, and then increased as a result of blood reinfusion. Platelet count, prothrombin time, and fibrinogen levels were similar for all groups. In the gelatine group arachidonic acid-induced platelet activation was decreased at T2 and T3 for maximal intensity, and at T2 for velocity. Platelet activation was unaltered in the PRP group. The CFRs disappeared during the CFR2 and 3 periods in the PRP group. The CFRs also disappeared during CFR2 in the gelatin group, but reappeared after reinfusion (CFR3). Bleed time was increased in both experimental groups, and in the gelatin group, there was a significant increase in spleenic bleeding, even after reinfusion.

Discussion

Low hematocrit levels induced an antithrombotic effect in this rabbit model. Blood transfusion reversed the effect. Hemodilution prolonged, and increased, the volume of bleeding. Reinfusion did not correct this. In this study, platelet aggregation occurred in PRP with no erythrocytes. Ear immersion bleed time is the only global test that assesses hemostasis (in the rabbit). Lengthened bleed times were observed in the PRP and GEL groups. These results may be relevant in humans because of the use of normovolemic hemodilution techniques are commonly used.

References

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