Changes in Thrombin Generation following Severe Hemorrhage and LR Resuscitation in Pigs

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The use of Army medical and/or other Army records in the preparation of this material is acknowledged, but is not to be construed as implying official Department of the Army approval of the conclusions presented.

Introduction

Hemorrhage accounts for about 50% of the deaths on conventional battlefields and is a major cause of death in civilian trauma. One of the most serious complications following hemorrhage is the disruption of hemostasis, resulting in the clinical consequences of uncontrolled bleeding, disseminated intravascular coagulation (DIC), and thrombotic complications. Thrombin catalyzes clot formation from fibrinogen and is generated upon the activation of various coagulation factors. Changes of thrombin generation kinetics following severe hemorrhage have not been described. This study investigated changes in thrombin generation kinetics after severe hemorrhage and LR resuscitation in pigs.

Methods

- Twelve pigs were randomized to normal control (C, n=6) and hemorrhage groups (H, n=6).
- Hemorrhage was induced in the H group by removal of approximately 60% of estimated blood volume exponentially using a computer controlled pump via the femoral artery over 1 hour, followed by resuscitation with Lactated Ringer's solution (LR, 3 times bled volume).
- Blood samples were taken at baseline and 6h after hemorrhage and resuscitation for measurements of fibrinogen levels, platelet counts, and activated clotting times (using Hemochron®). Thrombin generation was assessed as thrombin - antithrombin III (TAT) complex quantified from fresh whole blood samples taken at 6h post hemorrhage and resuscitation.
- All results are expressed as means ± SE. Comparison between the groups was made with Student's t-test. Comparisons over time were made using Bonferroni's multiple comparisons test with repeated measures. Statistical significance level was set at p< 0.05.

Results

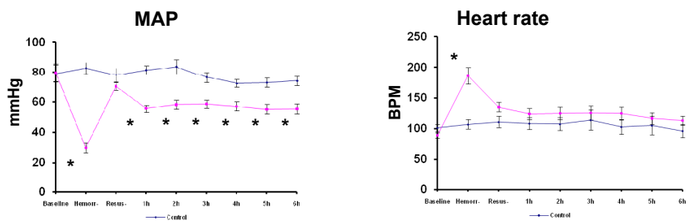

Fig 1 Hemodynamic changes following hemorrhage in pigs

* p<0.05 compared to baseline

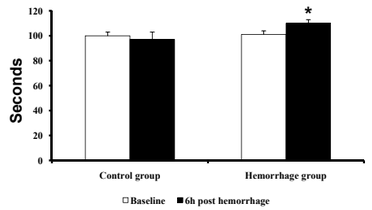

Fig 3 Changes in activated clotting times following severe hemorrhage in pigs

* p<0.05 compared to baseline

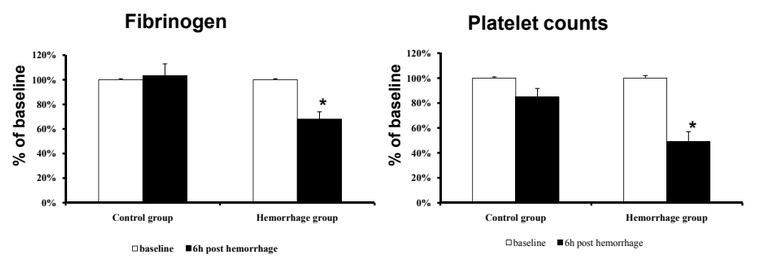

Fig 2 Changes in fibrinogen and platelet counts following hemorrhage in pigs

* p<0.05 compared to baseline

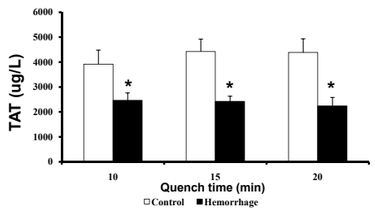

Fig 4 Changes in thrombin generation following severe hemorrhage in pigs

* p<0.05 compared to control

- There were no changes observed in any hemodynamic or coagulation values in the control group during the study
- Mean arterial pressure was decreased by hemorrhage and returned to baseline values immediately after resuscitation, but then fell below baseline for the remainder of the study. Heart rate was increased by hemorrhage but returned to baseline values after resuscitation (Fig 1)
- After hemorrhage and resuscitation, fibrinogen concentration decreased from baseline of 183±8 mg/dL to 100±5 mg/dL and platelet counts decreased from baseline of 424±58 10^3/µL to 210±30 10^3/µL (both p<0.05, Fig 2)
- Hemorrhage and resuscitation prolonged activated clotting times (Fig 3)
- Compared with control, thrombin generation was decreased to 68±6%, 59±8% and 50±2% at 10, 15, and 20 min of assay quench times, respectively (all p<0.05, Fig 4).

Conclusions

Severe hemorrhage and LR resuscitation caused comparable decreases in fibrinogen levels, platelet counts, and thrombin generation. These data suggest that supplementation of fibrinogen together with coagulation factors to restore coagulation function following severe blood loss may be beneficial.