Effect of Plasma Exosomes in Polymicrobial Sepsis on Erythrocyte Deformability

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Sepsis affects microcirculation and tissue perfusion leading to tissue hypoxia and multiple organ dysfunction. Red blood cells (RBCs) play the critical role of tissue oxygenation, thus functional changes in RBCs influence the outcome following sepsis. RBCs are easily deformable facilitating trafficking through capillaries; RBC rigidity adversely affects tissue oxygenation. The purpose of this project was to determine RBC deformability in a murine model of polymicrobial sepsis through a method using laser diffraction and microfluidics, and to identify the causative factor for RBC deformability in the plasma. The project tested the hypothesis that sepsis induces a decrease in RBC deformability and that plasma factors are important in imparting rigidity to the RBCs. Blood and tissue samples from mice subjected to the cecal ligation and puncture (CLP) model of sepsis were used. RBC deformability was tested using Rheoscan-D under shear stress of 0-20 Pascals. Normal RBCs were treated with plasma exosome-enriched extracellular vesicles and the effect on RBC deformability was determined. miRNA expression levels in exosomes were compared between sham and CLP-operated mice. The experiments demonstrated a significant decrease in RBC deformability following sepsis at shear pressure of 3 Pascals. RBC deformability recovered in sham operated mice by the third day, but not in CLP mice. Exosomes from CLP mice significantly decreased deformability of RBCs. miRNAs in the exosomes of sham and sepsis mice revealed a significant difference in expression profile. In conclusion, RBC deformability was decreased in sepsis, the acquired rigidity may have an adverse effect on microcirculation. Furthermore, exosomal vesicles were found to be a causative factor in reducing RBC deformability.