Analysis of the structural and mechanical effects of pro-thrombotic agents on neonatal fibrin networks following cardiopulmonary bypass.

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Bleeding is a serious complication of neonates undergoing cardiopulmonary bypass (CPB) and is associated with substantial morbidity and mortality. Mitigating bleeding is currently addressed through the transfusion of adult blood products including platelets and cryoprecipitate (fibrinogen component). However, significant differences exist between neonatal and adult clotting components, specifically fibrinogen. Our recent studies have shown that neonatal fibrinogen does not fully integrate with adult fibrinogen and leads to decreased susceptibility to fibrinolysis, compared to baseline neonatal clots. These differences could lead to increased thrombotic risks, therefore, a need exists to identify more safe and effective methods to promote clotting in neonates. Pro-coagulant agents, Prothrombinase Complex Concentrate (PCC) and recombinant activated factor VII (rFVIIa), are increasingly being used off-label to treat bleeding after cardiac surgery. Because these factors would stimulate endogenous neonatal fibrin formation, we hypothesize that the addition of these factors to post-CPB plasma will better recapitulate native neonatal clot properties than cryoprecipitate. Here we analyzed the structural, mechanical, and degradation properties of post-CPB neonatal clots formed in the presence of PCC, rFVIIa, or cryoprecipitate. The ex vivo addition of PCC and rFVIIa to post-CPB neonatal plasma resulted in an enhanced post-operative clot network with differences in fibrin alignment and mechanical and degradation properties (Figure 1). Our results suggest that these pro-coagulant agents could be used as an alternative to the transfusion of adult blood products for the treatment of post-CPB bleeding in neonates.

Figure 1: (A) Structural analysis was conducted with confocal microscopy of neonatal clots formed from baseline, post-bypass, post-transfusion (top), and post-bypass in the presence of increasing PCC (middle) or rFVIIa (bottom). (B) Average fibrin alignment values for all groups. N=8. Mechanical properties of clots were analyzed through AFM to determine clot stiffness (C). N=8-12. A custom microfluidics device was employed to evaluate clot degradation parameters (D) Top view of device with device blocked. (F) Image of microfluidics system set up on microscope. (F) Frame of clot boundary that is monitored over 32 hour period and degradation data (G) N=3.

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