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FIBRINOGEN IN INFANTS: DOES IT WORK?

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Introduction: Older literature suggests that the fibrinogen of infants may exist in a dysfunctional “fetal” variety that, despite quantitative levels similar to those of adults, could impair clot formation. This could also help explain the apparent importance of replacing fibrinogen in managing coagulopathies after cardiopulmonary bypass in children. Recent adult studies have shown that fibrinogen’s contribution to clotting can be determined by the use of modified thromboelastography (TEG). The maximum amplitude (MA) of a TEG tracing is determined by the number and function of both platelets and fibrinogen. Adding abciximab, a platelet glycoprotein IIb/IIIa receptor blocker that inhibits platelet-fibrinogen interaction and thus platelet aggregation, to whole blood (WB) during TEG measurements produces an MA value which should reflect only fibrinogen’s role in clot formation. This abciximab-modified MA value correlates with fibrinogen levels in adults. (1,2) We hypothesize that since adult and infant fibrinogen levels are similar, (3) the abciximab-modified MA value should also correlate with MA values in infants if their fibrinogen functions normally.

Methods: After IRB approval, 250 children scheduled for elective cardiac surgery and not taking medications with effects on the coagulation system were enrolled to obtain 50 children in each of 5 age groups: < 1 month, 1-3 months, 3-6 months, 6-12 months, and 12-14 months. Fibrinogen levels and platelet counts were obtained preoperatively and tissue factor (TF)-activated TEGs with and without abciximab (ReoPro[®]) were obtained after line placement in the operating room. TEGs without abciximab (TEGWB) were acquired by mixing 350 mL of WB with 10 mL of 1% TF in preheated disposable cups of a Thrombelastograph Coagulation Analyzer[®] (Haemoscope Corp., Skokie, IL). TEGs with abciximab (TEGFIBR) were similarly acquired by mixing 330 mL of WB with 10 mL of 1% TF, 5 mL of ReoPro[®] (2mg/mL), and 20 mL of 0.2M CaCl₂. MA values (in mm) were manually measured (without abciximab =

MAWB; with abciximab = MAFIBR) and elastic shear modulus was calculated [$G = (5000 * MA) / (100 - MA)$] (in dynes/cm²) since it is a more sensitive measure of clot strength (without abciximab = GWB; with abciximab = GFIBR). Differences between MAWB and MAFIBR (DMA) and GWB and GFIBR (DG) were calculated to assess platelet contribution to clotting. (1,2) ANOVA and two-sided t-tests with Bonferroni correction were used to compare groups and linear regression analysis was used to determine correlations.

Results: Fibrinogen levels were similar among groups except for being lower in the 3-6 month vs the 12-24 month age group. Fibrinogen levels correlated with MAWB and GWB only in age groups older than 3 months. More importantly, fibrinogen levels correlated with MAFIBR (p=0.009) and GFIBR (p=0.034) only in children older than 12 months. Platelet counts were significantly lower in the <1 month group vs all others but otherwise were similar among other groups. In children younger than 12 months, the only correlations with platelet count were with MAWB in children <1 month (p=0.031) and with DG in those 3-6 months old (p=0.031). However, in the 12-24 month group, platelet count correlated with MAWB (p=0.002), GWB (p=0.016), DMA (p=0.021), and DG (p=0.014).

Discussion: In adults, fibrinogen levels correlate weakly with MAWB and strongly with MAFIBR. (1,2) In children, the delay in correlation of fibrinogen levels with MAWB until >3 months of age and especially with MAFIBR until >12 months of age, and the weakness of these correlations, is different from that seen in adults and may very well indicate that fibrinogen exists in a dysfunctional form early in life. Additionally, the only consistent correlation of platelet count in adults is with DG. (1,2) In children this correlation exists in isolation in the 3-6 month group, does not exist in the 6-12 month group, and exists in conjunction with other correlations after 12 months. These findings may represent further functional immaturity in the coagulation process of infants.

References:

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