

SCA 9

THROMBIN GENERATION DURING CARDIOPULMONARY BYPASS IN NEONATES: ARE WE SUPPRESSING IT?

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Introduction: The adequacy of anticoagulation during cardiopulmonary bypass (CPB) can be assessed by the extent to which heparin attenuates the formation and activation of thrombin. Because heparin effect has been shown to be dependent on coupling with antithrombin III (ATIII) in adults(1) and because there are significant quantitative deficiencies in AT III during the neonatal period(2), adequate heparinization and suppression of thrombin formation in neonates is a concern. This investigation proposes to evaluate the adequacy of heparinization in neonates surrounding the CPB period as compared to an older population by measuring heparin levels, thrombin formation, and thrombin activity.

Methods: 10 neonates and 10 children ten years of age or older were enrolled after obtaining informed parental consent. Baseline celite and kaolin ACT values and baseline AT III levels were measured. Three minutes after heparin 400 units/kg, ACT values were repeated. Plasma heparin levels were measured by an anti-factor Xa chromogenic substrate assay at baseline, 30 minutes after full flow CPB, immediately after separation from CPB, and 3 and 24 hours after the completion of CPB. Prothrombin fragment 1.2 (PT1.2), a marker of thrombin formation, and fibrinopeptide A (FPA), a marker of thrombin activity, were likewise measured at the above intervals by enzyme-linked immunosorbent assays.

Results: Anti-factor Xa levels began at zero and returned to zero after protamine administration in both groups, but were significantly lower during CPB in the neonatal group (CPB on: 2.6 +/- .34 u/ml neonates vs. 3.9 +/- .38 u/ml older children; CPB off: 2.5 +/- .32 u/ml neonates vs. 4.3 +/- .51 u/ml older children). PT1.2 and FPA levels in neonates were significantly higher (p<0.05) at baseline, fell with the commencement of CPB, and dramatically rose to levels higher than those in the older children after CPB.

Conclusion: The data show that with a constant unit/kg dosage of heparin, neonates exhibit lower plasma heparin levels during CPB as measured by anti-factor Xa. The significantly higher baseline levels of PT1.2 and FPA present in neonates indicate early preoperative activation of their coagulation systems as compared to the older children. Although PT1.2 and FPA levels initially decrease

with the commencement of CPB, probably representing hemodilution, the subsequent rise in these markers indicates significantly more thrombin formation during and after CPB. These results support our concern that heparinization for CPB at standard doses of 400 units/kg may be inadequate in neonates to suppress thrombin generation and activity.

References:

- 1) Anesth Analg 1997;85:498-506
- 2) Am J Pediatr Hematol Oncol 1990;12(1):95-104

